IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Timothy A. Coleman

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Application No.: 09/921,143

Group Art Unit: 1653

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Examiner: Not Yet Assigned

For: Vascular Endothelial Growth Factor 2

SUBMISSION OF REPLACEMENT/SUBSTITUTE DRAWINGS

Attn: Draftsperson
Commissioner for Patents
Washington, DC 20231

Sir:

Applicants submit herewith replacement/substitute Figures 1A-31U (68 sheets) to replace Figures 1A-31G (47 sheets) as originally filed. Additional pages are due to reorganization of the drawings in order to comply with the margin requirements under 37 C.F.R. § 1.84. No new matter is introduced.

No fee is believed due for this submission. In the event that a fee is required in connection with this submission, please charge the required fee to Deposit Account No. 08-3425.

Respectfully submitted,

Dated: April 17, 2003

Melissa J. Pytel
Registration No. 41,512
HUMAN GENOME SCIENCES, INC.
9410 Key West Avenue
Rockville, Maryland 20850
(301) 610-5764
Attorney for Applicants

```
                GTCCTTCCACCATGCACTCGCTGGGCTTCTTCTCTGTGGCGTGTTCTCTGCTCGCCGCTG
1               --------+---------+---------+---------+---------+---------+         60
                CAGGAAGGTGGTACGTGAGCGACCCGAAGAAGAGACACCGCACAAGAGACGAGCGGCGAC
                          M  H  S  L  G  F  F  S  V  A  C  S  L  L  A  A  A

                CGCTGCTCCCGGGTCCTCGCGAGGCGCCCGCCGCCGCCGCCGCCTTCGAGTCCGGACTCG
61              --------+---------+---------+---------+---------+---------+        120
                GCGACGAGGGCCCAGGAGCGCTCCGCGGGCGGCGGCGGCGGCGGAAGCTCAGGCCTGAGC
                  L  L  P  G  P  R  E  A  P  A  A  A  A  A  F  E  S  G  L  D

                ACCTCTCGGACGCGGAGCCCGACGCGGGCGAGGCCACGGCTTATGCAAGCAAAGATCTGG
121             --------+---------+---------+---------+---------+---------+        180
                TGGAGAGCCTGCGCCTCGGGCTGCGCCCGCTCCGGTGCCGAATACGTTCGTTTCTAGACC
                  L  S  D  A  E  P  D  A  G  E  A  T  A  Y  A  S  K  D  L  E

                AGGAGCAGTTACGGTCTGTGTCCAGTGTAGATGAACTCATGACTGTACTCTACCCAGAAT
181             --------+---------+---------+---------+---------+---------+        240
                TCCTCGTCAATGCCAGACACAGGTCACATCTACTTGAGTACTGACATGAGATGGGTCTTA
                  E  Q  L  R  S  V  S  S  V  D  E  L  M  T  V  L  Y  P  E  Y

                ATTGGAAAATGTACAAGTGTCAGCTAAGGAAAGGAGGCTGGCAACATAACAGAGAACAGG
241             --------+---------+---------+---------+---------+---------+        300
                TAACCTTTTACATGTTCACAGTCGATTCCTTTCCTCCGACCGTTGTATTGTCTCTTGTCC
                  W  K  M  Y  K  C  Q  L  R  K  G  G  W  Q  H  N  R  E  Q  A

                CCAACCTCAACTCAAGGACAGAAGAGACTATAAAATTTGCTGCAGCACATTATAATACAG
301             --------+---------+---------+---------+---------+---------+        360
                GGTTGGAGTTGAGTTCCTGTCTTCTCTGATATTTTAAACGACGTCGTGTAATATTATGTC
                  N  L  N  S  R  T  E  E  T  I  K  F  A  A  A  H  Y  N  T  E
```

FIG. 1A

MATCH WITH FIG. 1B

MATCH WITH FIG. 1A

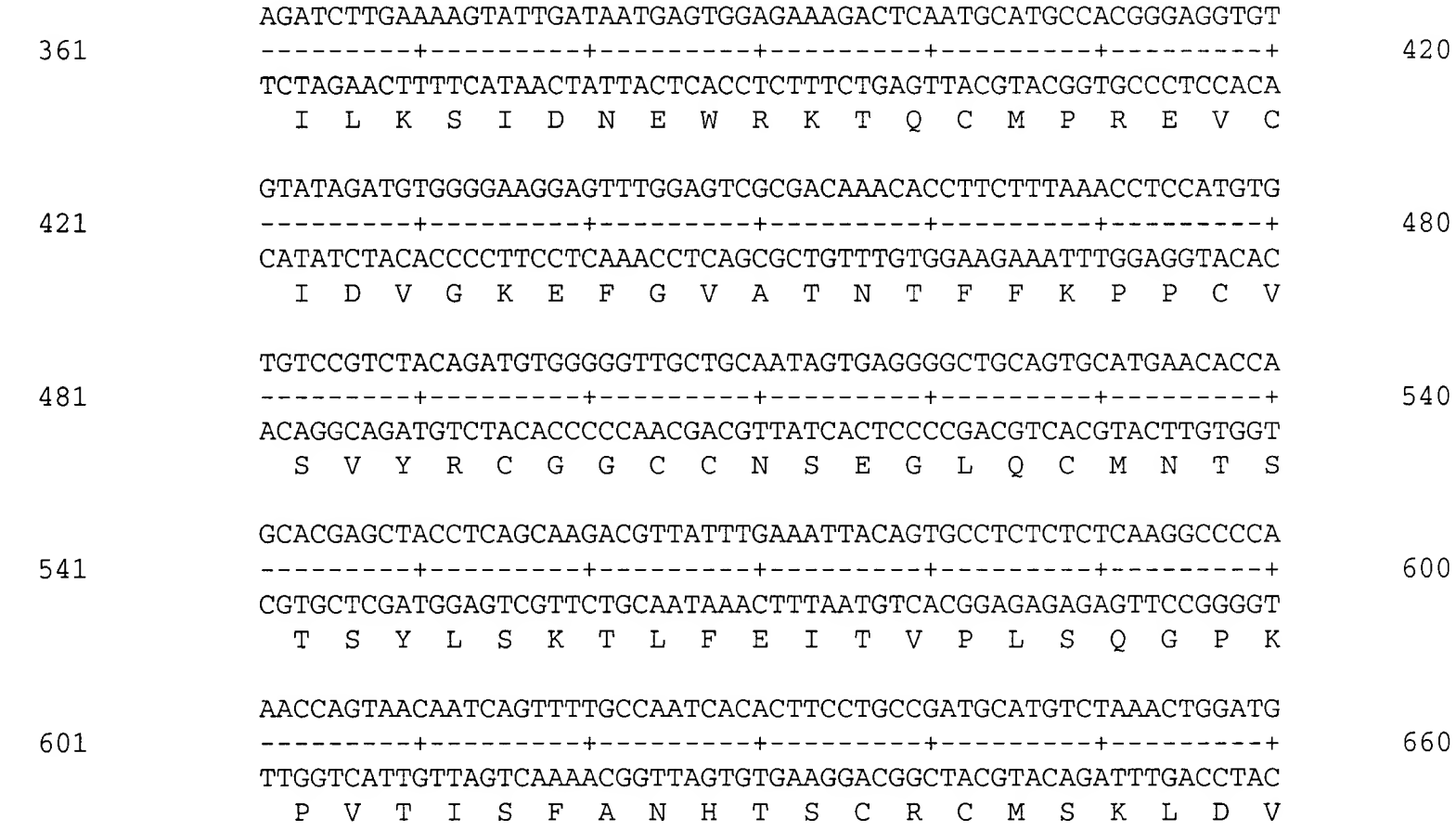


FIG. 1B

MATCH WITH FIG. 1C

MATCH WITH FIG. 1B

```
                TTTACAGACAAGTTCATTCCATTATTAGACGTTCCCTGCCAGCAACACTACCACAGTGTC
661             ---------+---------+---------+---------+---------+---------+       720
                AAATGTCTGTTCAAGTAAGGTAATAATCTGCAAGGGACGGTCGTTGTGATGGTGTCACAG
                  Y  R  Q  V  H  S  I  I  R  R  S  L  P  A  T  L  P  Q  C  Q

                AGGCAGCGAACAAGACCTGCCCCACCAATTACATGTGGAATAATCACATCTGCAGATGCC
721             ---------+---------+---------+---------+---------+---------+       780
                TCCGTCGCTTGTTCTGGACGGGGTGGTTAATGTACACCTTATTAGTGTAGACGTCTACGG
                  A  A  N  K  T  C  P  T  N  Y  M  W  N  N  H  I  C  R  C  L

                TGGCTCAGGAAGATTTTATGTTTTCCTCGGATGCTGGAGATGACTCAACAGATGGATTCC
781             ---------+---------+---------+---------+---------+---------+       840
                ACCGAGTCCTTCTAAAATACAAAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGG
                  A  Q  E  D  F  M  F  S  S  D  A  G  D  D  S  T  D  G  F  H

                ATGACATCTGTGGACCAAACAAGGAGCTGGATGAAGAGACCTGTCAGTGTGTCTGCAGAG
841             ---------+---------+---------+---------+---------+---------+       900
                TACTGTAGACACCTGGTTTGTTCCTCGACCTACTTCTCTGGACAGTCACACAGACGTCTC
                  D  I  C  G  P  N  K  E  L  D  E  E  T  C  Q  C  V  C  R  A

                CGGGGCTTCGGCCTGCCAGCTGTGGACCCCACAAAGAACTAGACAGAAACTCATGCCAGT
901             ---------+---------+---------+---------+---------+---------+       960
                GCCCCGAAGCCGGACGGTCGACACCTGGGGTGTTTCTTGATCTGTCTTTGAGTACGGTCA
                  G  L  R  P  A  S  C  G  P  H  K  E  L  D  R  N  S  C  Q  C
```

FIG. 1C

MATCH WITH FIG. 1D

MATCH WITH FIG. 1C

FIG. 1D

MATCH WITH FIG. 1E

MATCH WITH FIG. 1D

```
                AAATGAGCTAAGATTGTACTGTTTTCCAGTTCATCGATTTTCTATTATGGAAAACTGTGT
1261            ---------+---------+---------+---------+---------+---------+      1320
                TTTACTCGATTCTAACATGACAAAAGGTCAAGTAGCTAAAAGATAATACCTTTTGACACA
                  M   S   *

                TGCCACAGTAGAACTGTCTGTGAACAGAGAGACCCTTGTGGGTCCATGCTAACAAAGACA
1321            ---------+---------+---------+---------+---------+---------+      1380
                ACGGTGTCATCTTGACAGACACTTGTCTCTCTGGGAACACCCAGGTACGATTGTTTCTGT

                AAAGTCTGTCTTTCCTGAACCATGTGGATAACTTTACAGAAATGGACTGGAGCTCATCTG
1381            ---------+---------+---------+---------+---------+---------+      1440
                TTTCAGACAGAAAGGACTTGGTACACCTATTGAAATGTCTTTACCTGACCTCGAGTAGAC

                CAAAAGGCCTCTTGTAAAGACTGGTTTTCTGCCAATGACCAAACAGCCAAGATTTTCCTC
1441            ---------+---------+---------+---------+---------+---------+      1500
                GTTTTCCGGAGAACATTTCTGACCAAAAGACGGTTACTGGTTTGTCGGTTCTAAAAGGAG

                TTGTGATTTCTTTAAAAGAATGACTATATAATTTATTTCCACTAAAAATATTGTTTCTGC
1501            ---------+---------+---------+---------+---------+---------+      1560
                AACACTAAAGAAATTTTCTTACTGATATATTAAATAAAGGTGATTTTTATAACAAAGACG

                ATTCATTTTTATAGCAACAACAATTGGTAAAACTCACTGTGATCAATATTTTTATATCAT
1561            ---------+---------+---------+---------+---------+---------+      1620
                TAAGTAAAAATATCGTTGTTGTTAACCATTTTGAGTGACACTAGTTATAAAAATATAGTA

                GCAAAATATGTTTAAAATAAAATGAAAATTGTATTTATAAAAAAAAAAAAAAAA
1621            ---------+---------+---------+---------+---------+----      1674
                CGTTTTATACAAATTTTATTTTACTTTTAACATAAATATTTTTTTTTTTTTTTT
```

FIG. 1E

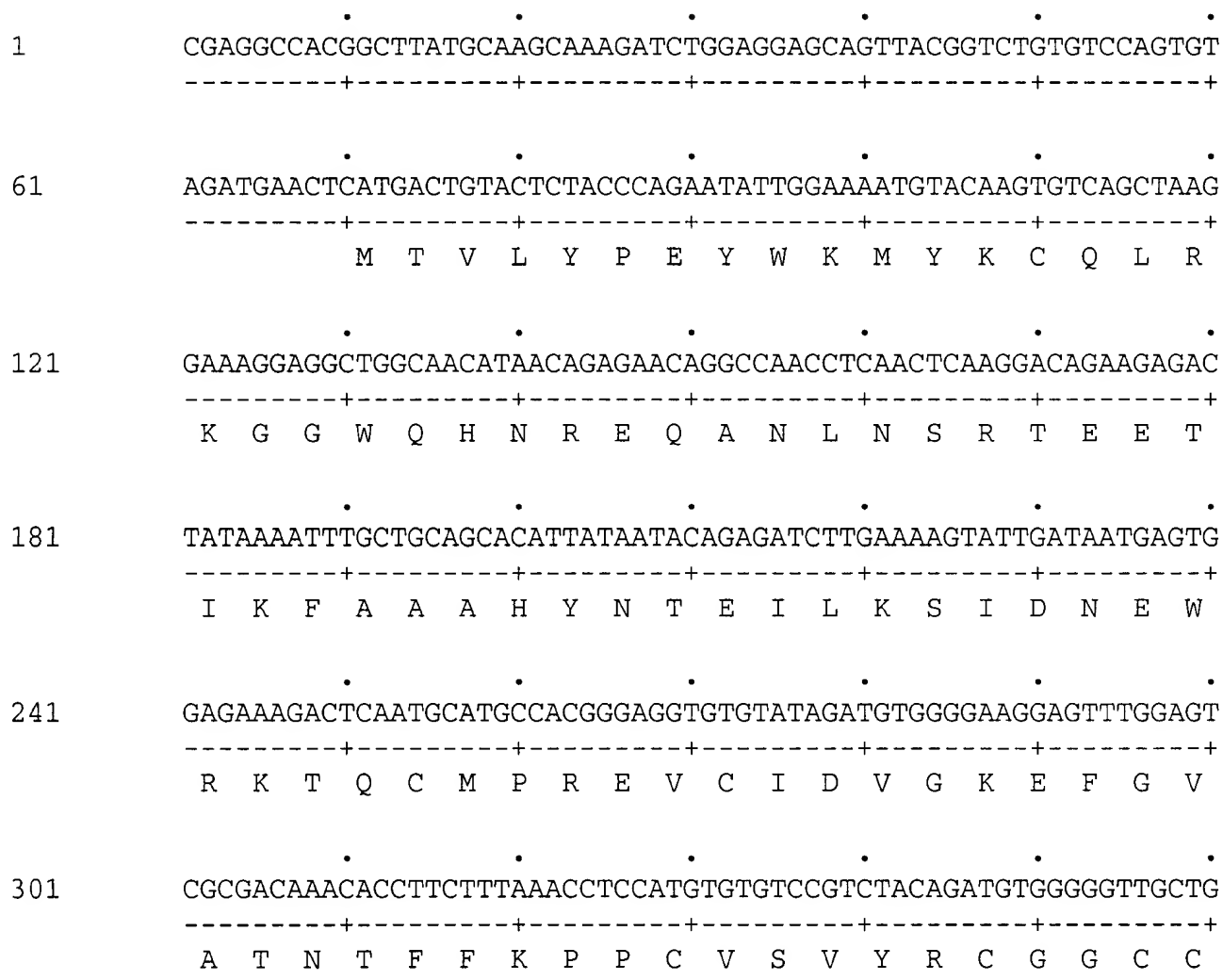


FIG. 2A

MATCH WITH FIG. 2B

MATCH WITH FIG. 2A

```
                .         .         .         .         .         .
421     TGAAATTACAGTGCCTCTCTCTCAAGGCCCCAAACCAGTAACAATCAGTTTTGCCAATCA
        ---------+---------+---------+---------+---------+---------+
         E  I  T  V  P  L  S  Q  G  P  K  P  V  T  I  S  F  A  N  H

                .         .         .         .         .         .
481     CACTTCCTGCCGATGCATGTCTAAACTGGATGTTTACAGACAAGTTCATTCCATTATTAG
        ---------+---------+---------+---------+---------+---------+
         T  S  C  R  C  M  S  K  L  D  V  Y  R  Q  V  H  S  I  I  R

                .         .         .         .         .         .
541     ACGTTCCCTGCCAGCAACACTACCACAGTGTCAGGCAGCGAACAAGACCTGCCCCACCAA
        ---------+---------+---------+---------+---------+---------+
         R  S  L  P  A  T  L  P  Q  C  Q  A  A  N  K  T  C  P  T  N

                .         .         .         .         .         .
601     TTACATGTGGAATAATCACATCTGCAGATGCCTGGCTCAGGAAGATTTTATGTTTTCCTC
        ---------+---------+---------+---------+---------+---------+
         Y  M  W  N  N  H  I  C  R  C  L  A  Q  E  D  F  M  F  S  S

                .         .         .         .         .         .
661     GGATGCTGGAGATGACTCAACAGATGGATTCCATGACATCTGTGGACCAAACAAGGAGCT
        ---------+---------+---------+---------+---------+---------+
         D  A  G  D  D  S  T  D  G  F  H  D  I  C  G  P  N  K  E  L

                .         .         .         .         .         .
721     GGATGAAGAGACCTGTCAGTGTGTCTGCAGAGCGGGGCTTCGGCCTGCCAGCTGTGGACC
        ---------+---------+---------+---------+---------+---------+
         D  E  E  T  C  Q  C  V  C  R  A  G  L  R  P  A  S  C  G  P
```

MATCH WITH FIG. 2C

FIG. 2B

MATCH WITH FIG. 2B

```
                .         .         .         .         .         .
781     CCACAAAGAACTAGACAGAAACTCATGCCAGTGTGTCTGTAAAAACAAACTCTTCCCCAG
        ---------+---------+---------+---------+---------+---------+
         H   K   E   L   D   R   N   S   C   Q   C   V   C   K   N   K   L   F   P   S

                .         .         .         .         .         .
841     CCAATGTGGGGCCAACCGAGAATTTGATGAAAACACATGCCAGTGTGTATGTAAAAGAAC
        ---------+---------+---------+---------+---------+---------+
         Q   C   G   A   N   R   E   F   D   E   N   T   C   Q   C   V   C   K   R   T

                .         .         .         .         .         .
901     CTGCCCCAGAAATCAACCCCTAAATCCTGGAAAATGTGCCTGTGAATGTACAGAAAGTCC
        ---------+---------+---------+---------+---------+---------+
         C   P   R   N   Q   P   L   N   P   G   K   C   A   C   E   C   T   E   S   P

                .         .         .         .         .         .
961     ACAGAAATGCTTGTTAAAAGGAAAGAAGTTCCACCACCAAACATGCAGCTGTTACAGACG
        ---------+---------+---------+---------+---------+---------+
         Q   K   C   L   L   K   G   K   K   F   H   H   Q   T   C   S   C   Y   R   R

                .         .         .         .         .         .
1021    GCCATGTACGAACCGCCAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGTGTG
        ---------+---------+---------+---------+---------+---------+
         P   C   T   N   R   Q   K   A   C   E   P   G   F   S   Y   S   E   E   V   C

                .         .         .         .         .         .
1081    TCGTTGTGTCCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTACTGTTTTCCA
        ---------+---------+---------+---------+---------+---------+
         R   C   V   P   S   Y   W   Q   R   P   Q   M   S   *
```

MATCH WITH FIG. 2D

FIG. 2C

MATCH WITH FIG. 2C

```
                .         .         .         .         .         .
1141    GTTCATCGATTTTCTATTATGGAAAACTGTGTTGCCACAGTAGAACTGTCTGTGAACAGA
        ---------+---------+---------+---------+---------+---------+

                .         .         .         .         .         .
1201    GAGACCCTTGTGGGTCCATGCTAACAAAGACAAAAGTCTGTCTTTCCTGAACCATGTGGA
        ---------+---------+---------+---------+---------+---------+

                .         .         .         .         .         .
1261    TAACTTTACAGAAATGGACTGGAGCTCATCTGCAAAAGGCCTCTTGTAAAGACTGGTTTT
        ---------+---------+---------+---------+---------+---------+

                .         .         .         .         .         .
1321    CTGCCAATGACCAAACAGCCAAGATTTTCCTCTTGTGATTTCTTTAAAAGAATGACTATA
        ---------+---------+---------+---------+---------+---------+

                .         .         .         .         .         .
1381    TAATTTATTTCCACTAAAAATATTGTTTCTGCATTCATTTTTATAGCAACAACAATTGGT
        ---------+---------+---------+---------+---------+---------+

                .         .         .         .         .         .
1441    AAAACTCACTGTGATCAATATTTTTATATCATGCAAAATATGTTTAAAATAAAATGAAAA
        ---------+---------+---------+---------+---------+---------+

                .         .
1501    TTGTATTATAAAAAAAAAAAAAAA
        ---------+---------+-----
```

FIG. 2D

```
          1                                                  50
Pdgfa .MRTLACLLL LGCGYLAHVL AEEAEIPREV IERLARSQIH SIRDLQRLLE
Pdgfb MNRCWA.LFL SLCCYLRLVS AEGDPIPEEL YEMLSDHSIR SFDDLQRLLH
 Vegf .....MNFLL SWVHWSLALL LY..... ..........  .LHHAKWSQA
Vegf2 .......MTV LYPEYWKMYK CQ..... ..........  .LRKGGWQHN

         51                                                 100
Pdgfa IDSVGSEDSL DTSLRAHGVH ATKHVPEKRP LPIRRKRSI. .....EEAVP
Pdgfb GDP.GEEDGA ELDLNMTRSH SGGELES... .LARGRRSLG SLTIAEPAMI
 Vegf APMAE..... ......GGGQ NHHEVVKFMD .VYQR..... ..........
Vegf2 REQANLNSRT EETIKFAAAH YNTEILKSID NEWRK..... ..........

         101                                                150
Pdgfa AVCKTRTVIY EIPRSQVDPT SANFLIWPPC VEVKRCTGCC NTSSVKCQPS
Pdgfb AECKTRTEVF EISRRLIDRT NANFLVWPPC VEVQRCSGCC NNRNVQCRPT
 Vegf SYCHPIETLV DIFQEYPDEI ..EYIFKPSC VPLMRCGGCC NDEGLECVPT
Vegf2 TQCMPREVCI DVGKEFGVAT ..NTFFKPPC VSVYRCGGCC NSEGLQCMNT

         151                                                200
Pdgfa RVHHRSVKVA KVEYVRKKPK LKEVQVRLEE HLECACC.... AT.......
Pdgfb QVQLRPVQVR KIEIVRKKPI FKKATVTLED HLACKCD.... ETVAAARPVT
 Vegf EESNITMQIM RIK.PH..QG QHIGEMSFLQ HNKCECRPKK DRARQEKKSV
Vegf2 STSYLSKTLF EIT.VPLSQG PKPVTISFAN HTSCRCMSKL DVYRQVHSII
```

FIG. 3A

```
      201                                                        250
Pdgfa ....TSLNPD YREEDTDVR. .......... .......... ..........
Pdgfb RSPGGSQEQR AKTPQTRVTI RTVRVRRPPK GKHRKFKHTH DKTALKETLG
 Vegf RGK....... .GKGQKRKRK KSRYKSWSVY VGARCCLMPW SLPGPHP...
Vegf2 RRSLPATLPQ CQAANKTCPT NYMWNNHICR CLAQEDFMFS SDAGDDSTDG

      251                                                        300
Pdgfa .......... .......... .......... .......... ..........
Pdgfb A......... .......... .......... .......... ..........
 Vegf ....CGP... .......... .......CSE RRKHLFVQDP QTCKCSCKNT
Vegf2 FHDICGPNKE LDEETCQCVC RAGLRPASCG PHKEL...DR NSCQCVCKNK

      301                                                        350
Pdgfa .......... .......... .......... .......... ..........
Pdgfb .......... .......... .......... .......... ..........
 Vegf ..DSRCKARQ LELNERTCRC DKPRR..... .......... ..........
Vegf2 LFPSQCGANR .EFDENTCQC VCKRTCPRNQ PLNPGKCACE CTESPQKCLL

      351                                                   398
Pdgfa .......... .......... .......... .......... ........
Pdgfb .......... .......... .......... .......... ........
 Vegf .......... .......... .......... .......... ........
Vegf2 KGKKFHHQTC SCYRRPCTNR QKACEPGFSY SEEVCRCVPS YWQRPQMS
```

FIG. 3B

PERCENTAGE (%) OF AMINO ACID IDENTITIES BETWEEN EACH PAIR OF GENES IS SHOWN IN THE FOLLOWING TABLE

	PDGFα	PDGFβ	VEGF	VEGF-2
PDGFα				
PDGFβ	48.0			
VEGF	20.7	22.7		
VEGF-2	23.5	22.4	30.0	

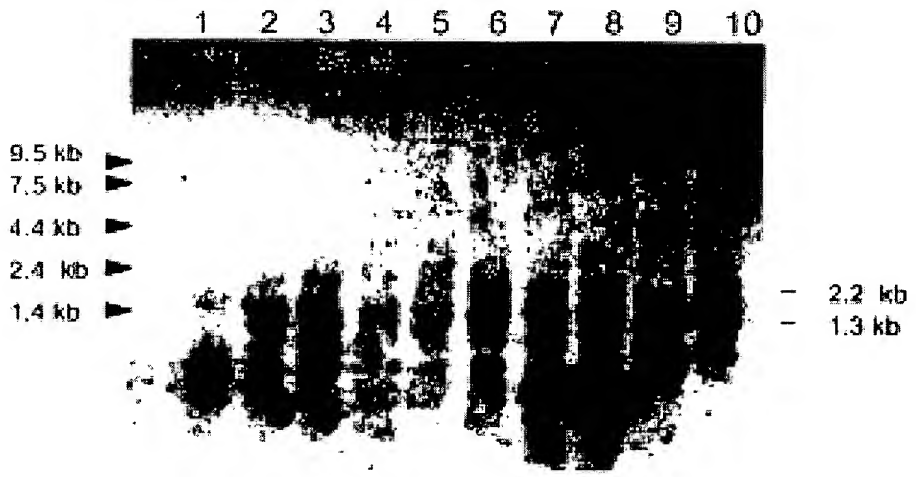
FIG. 4

Expression of VEGF2 mRNA in
Human Breast Tumor Cells

Lane 1. normal breast tissue
Lane 2. breast tumor tissue
Lane 3-9. breast tumor cell lines.

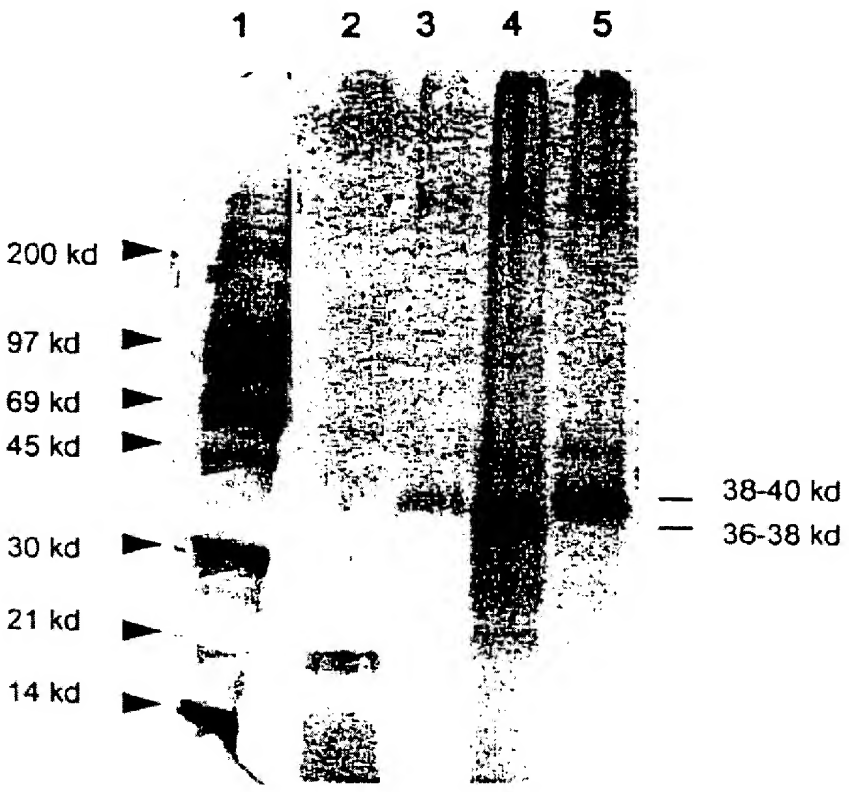
FIG. 5

Expression of VEGF-2 mRNA in Human Adult Tissues



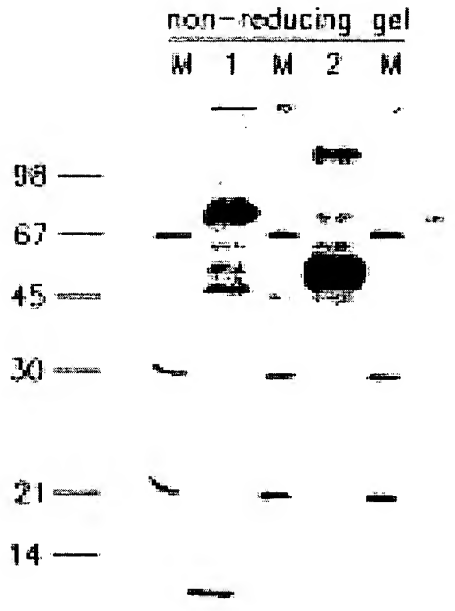
1.	Ovary	6.	Lung
2.	Testes	7.	Spleen
3.	Gall Blader	8.	Prostate
4.	Kidney	9.	Hippocampus
5.	Liver	10.	Heart

FIG. 6



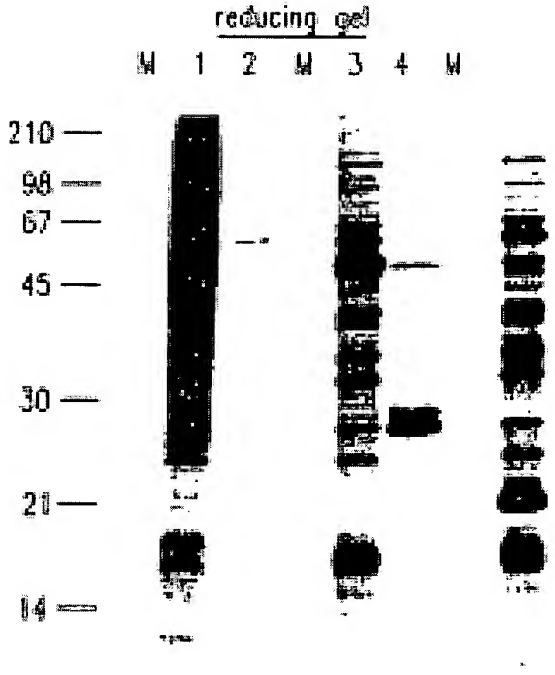
Lane 1: 14-C and rainbow M.W. marker
Lane 2: FGF control
Lane 3: VEGF2 (M13-reverse & forward primer)
Lane 4: VEGF2 (M13-reverse & VEGF-F4 primer)
Lane 5: VEGF2 (M13-reverse & VEGF-F5 primer)

FIG. 7



Lane M: Marker
Lane 1: Vector medium
Lane 2: VEGF2 medium

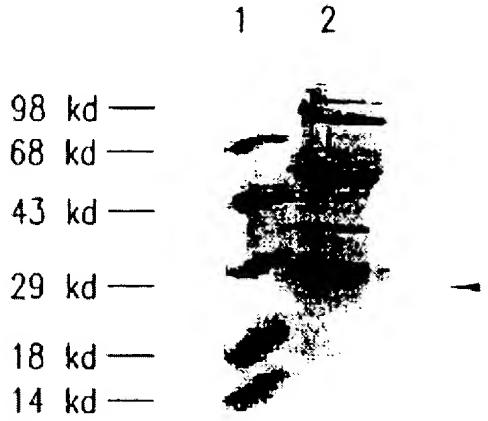
FIG. 8A



Lane M: Marker
Lane 1: vector cytoplasm
Lane 2: vector medium
Lane 3: VEGF2 cytoplasm
Lane 4: VEGF2 medium

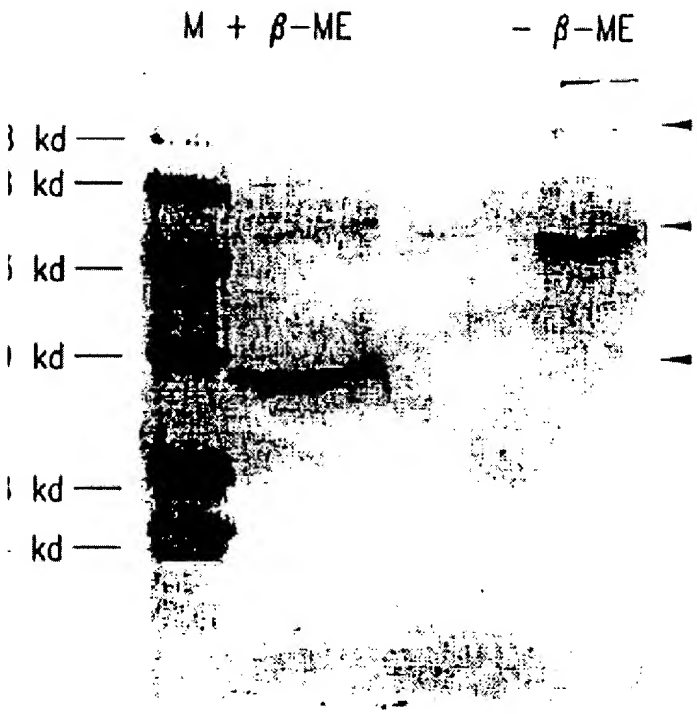
FIG. 8B

FIG. 9



Lane 1: Molelular weight marker
Lane 2: Precipitates containing VEGF2.

FIG. 10



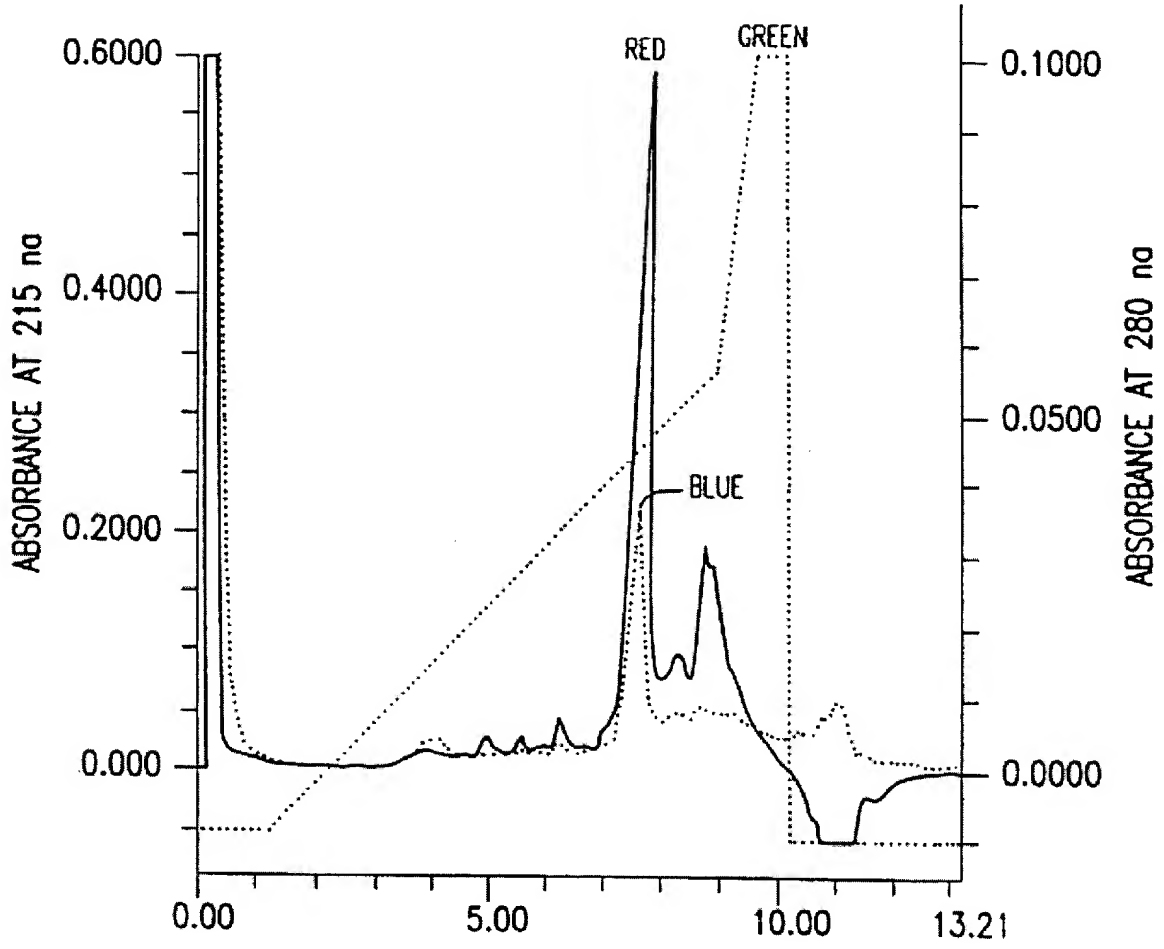


FIG. 11

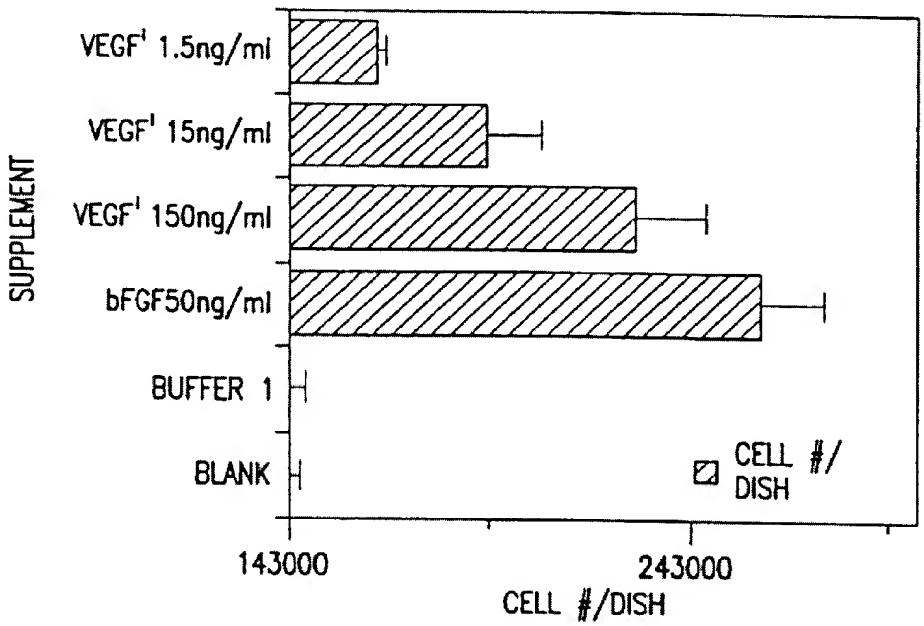


FIG. 12

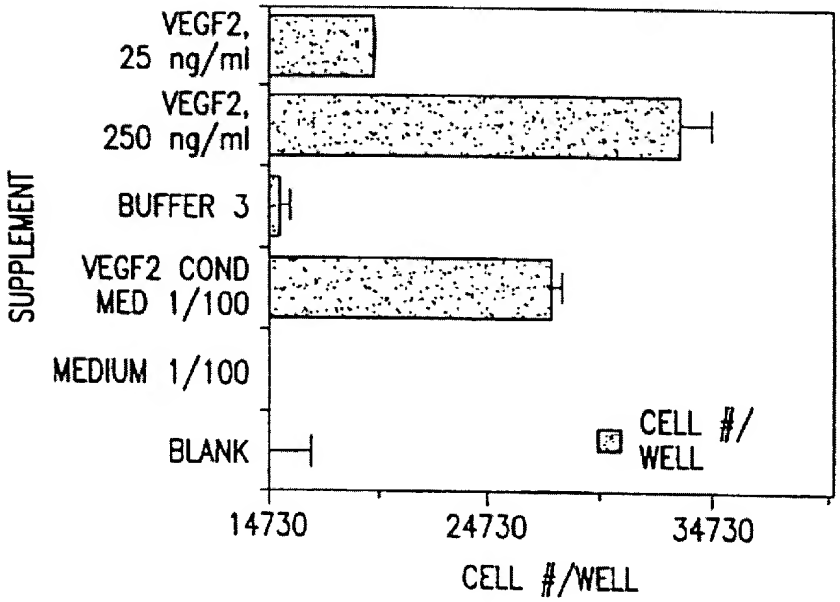


FIG. 13

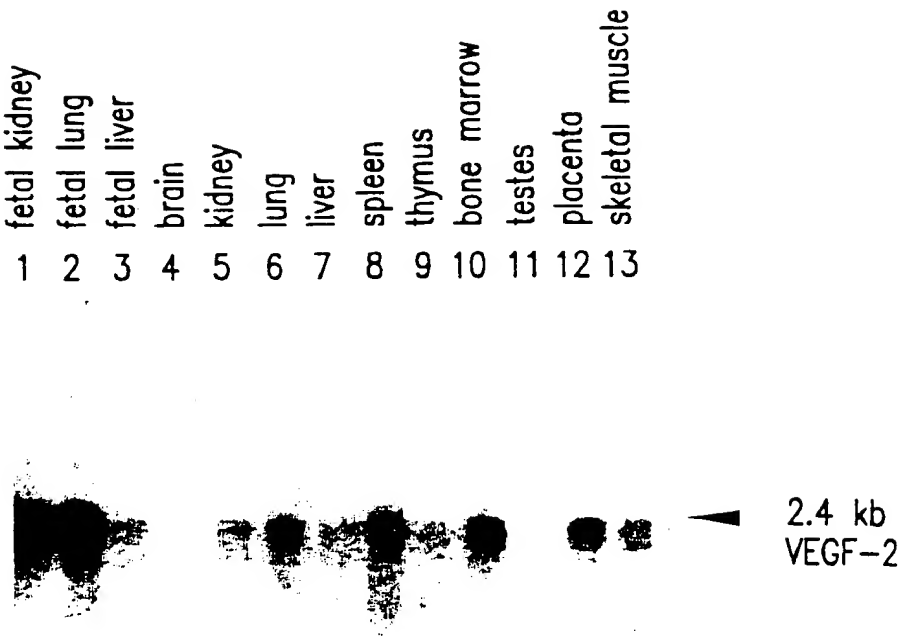
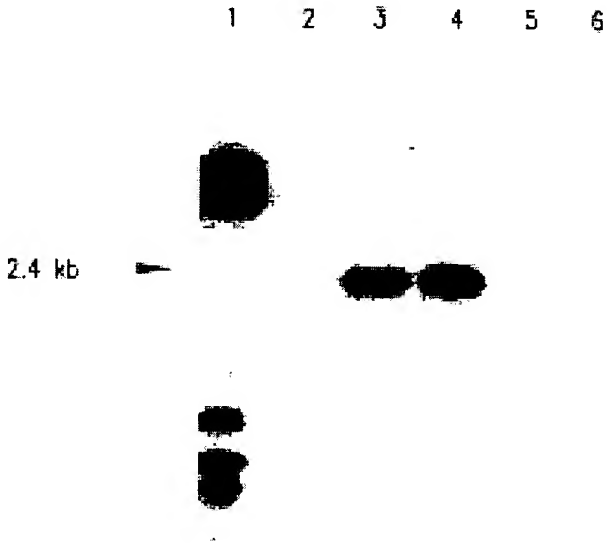


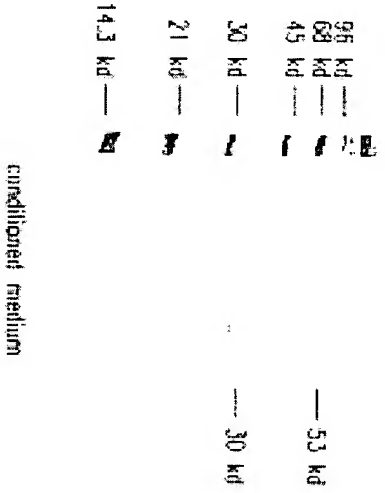
FIG. 14A

FIG. 14B



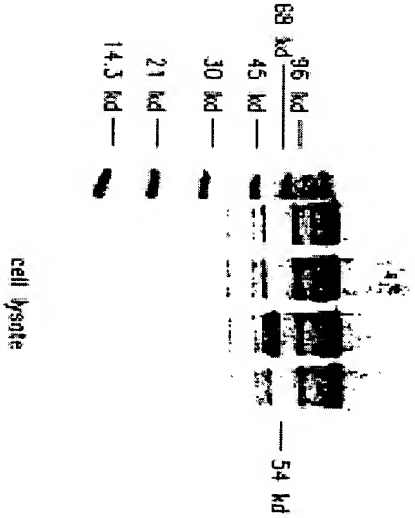
1. Molecular weight marker
2. Umbelical vein endothelial cells
3. Aortic smooth muscle cells
4. Dermal fibroblast

FIG. 15



1. Molecular weight marker
2. Blank
3. Control protein-HA
4. Vector control
5. VEGF2-HA

FIG. 16A



1. Molecular weight marker
2. Blank
3. Control protein-HA
4. VEGF2-HA
5. Vector control

FIG. 16B

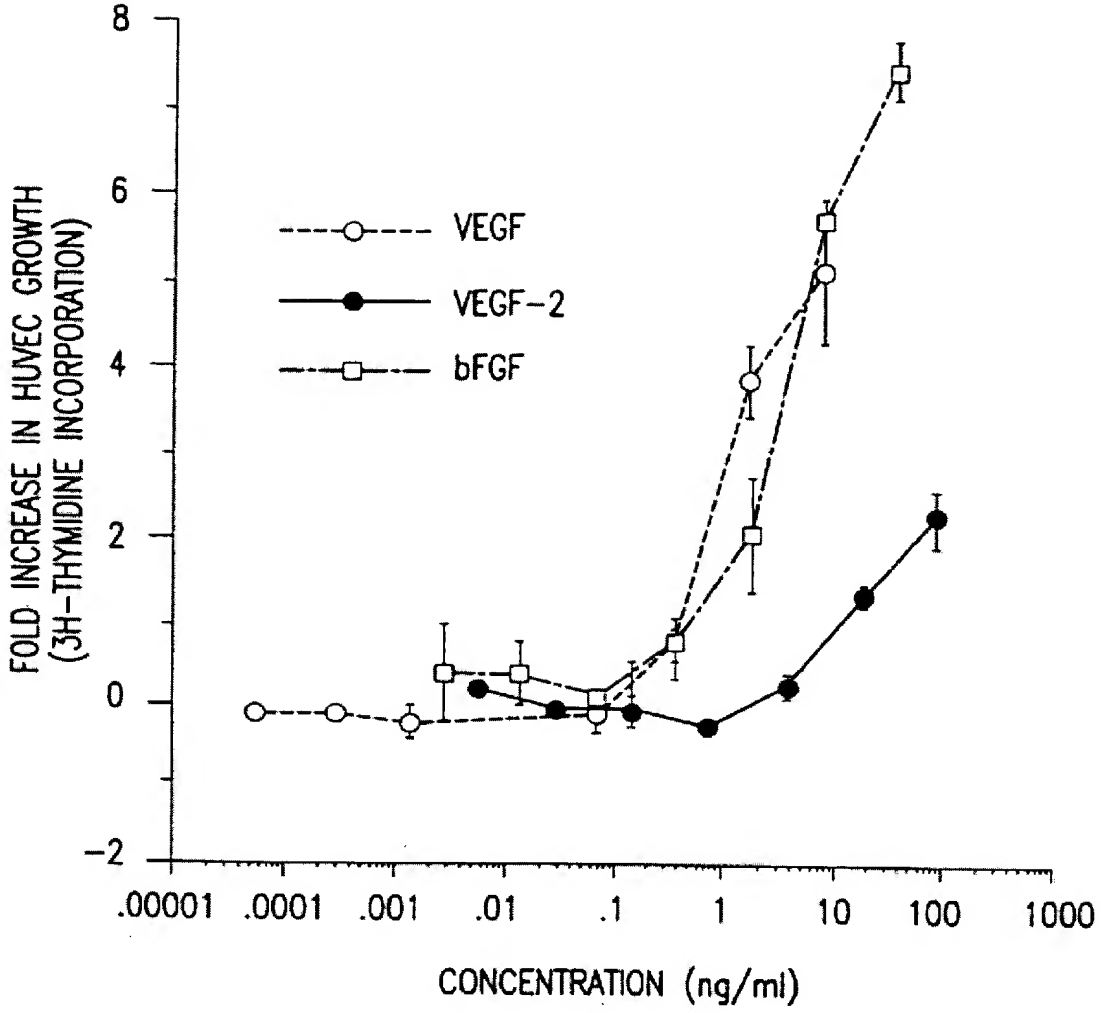


FIG. 17

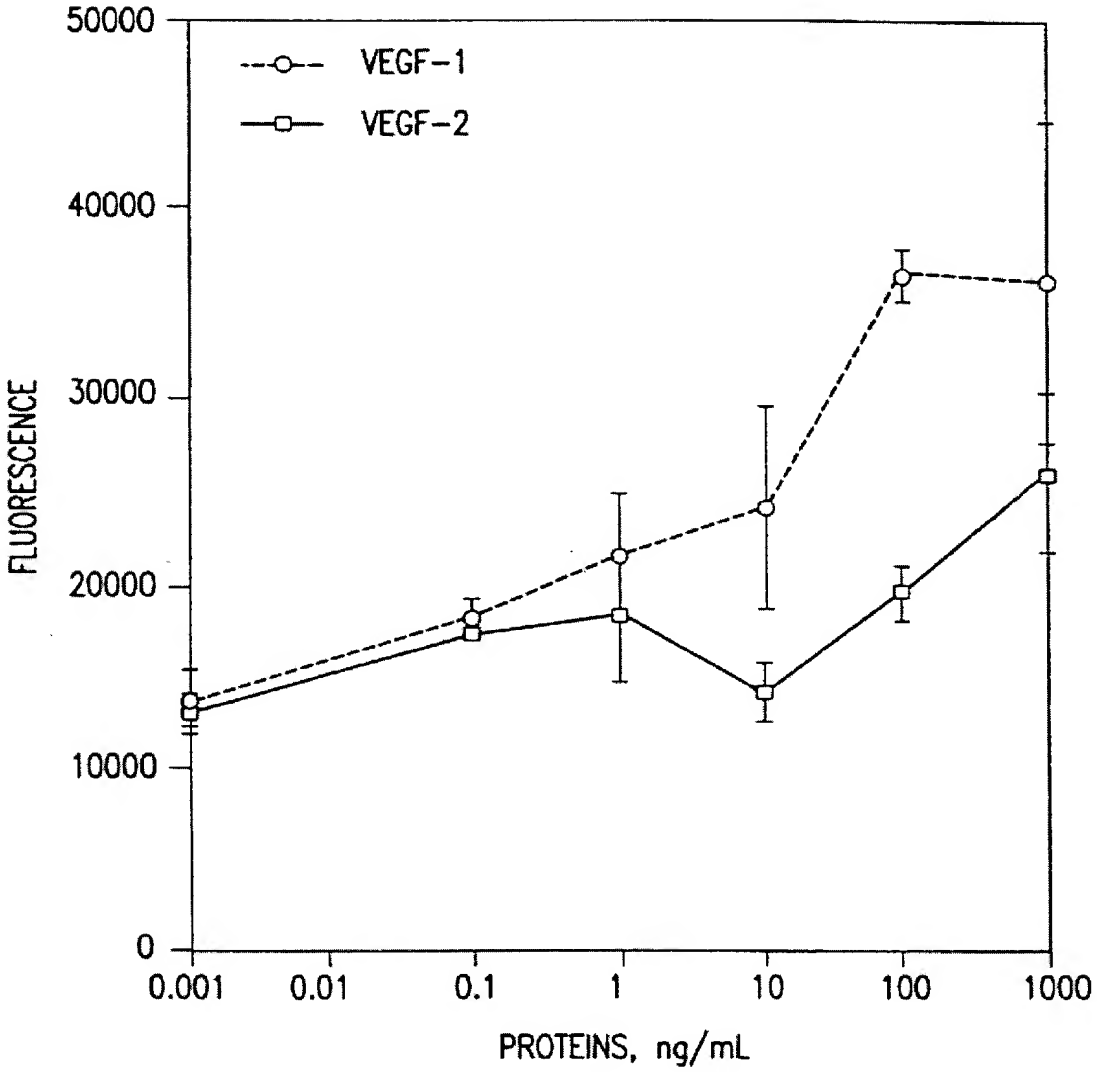


FIG. 18

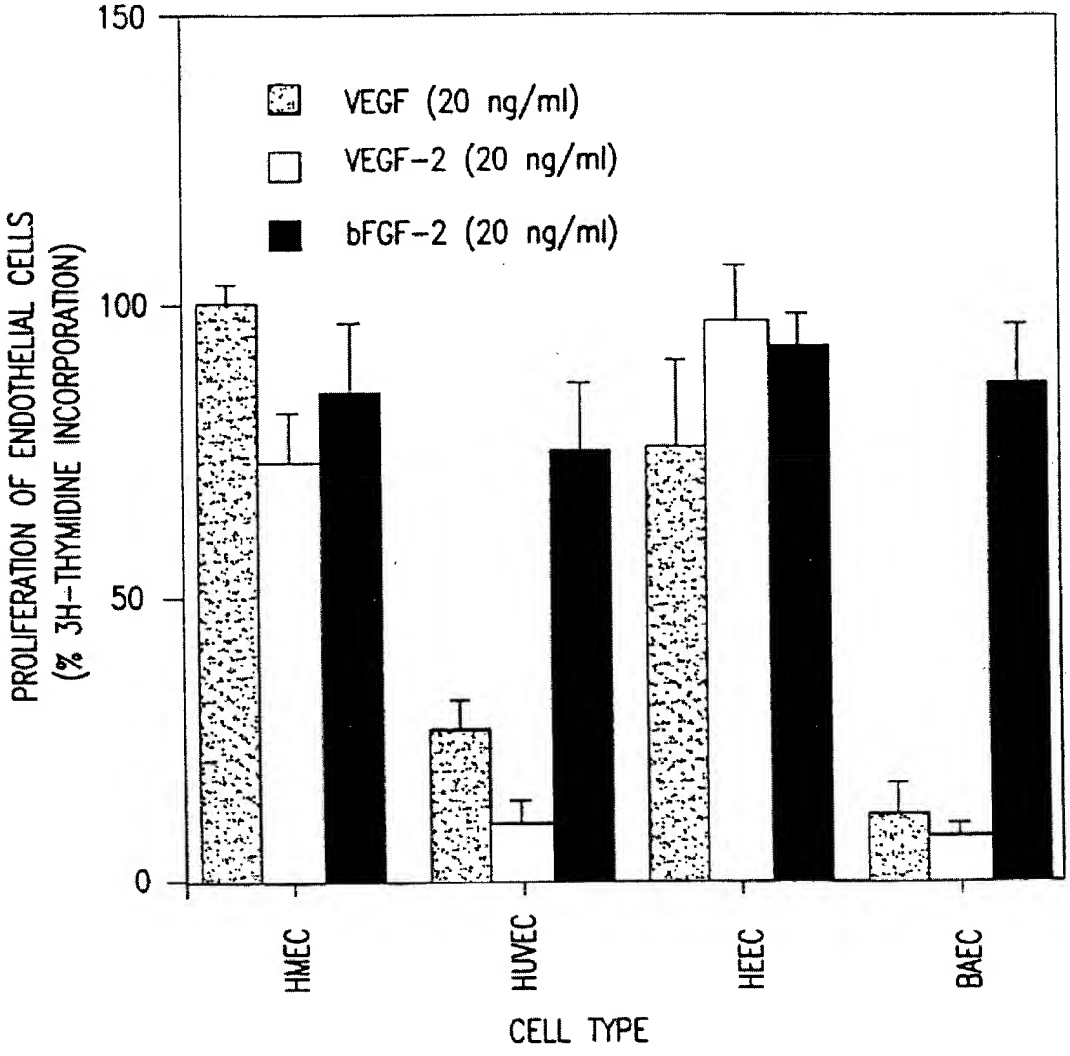


FIG. 19

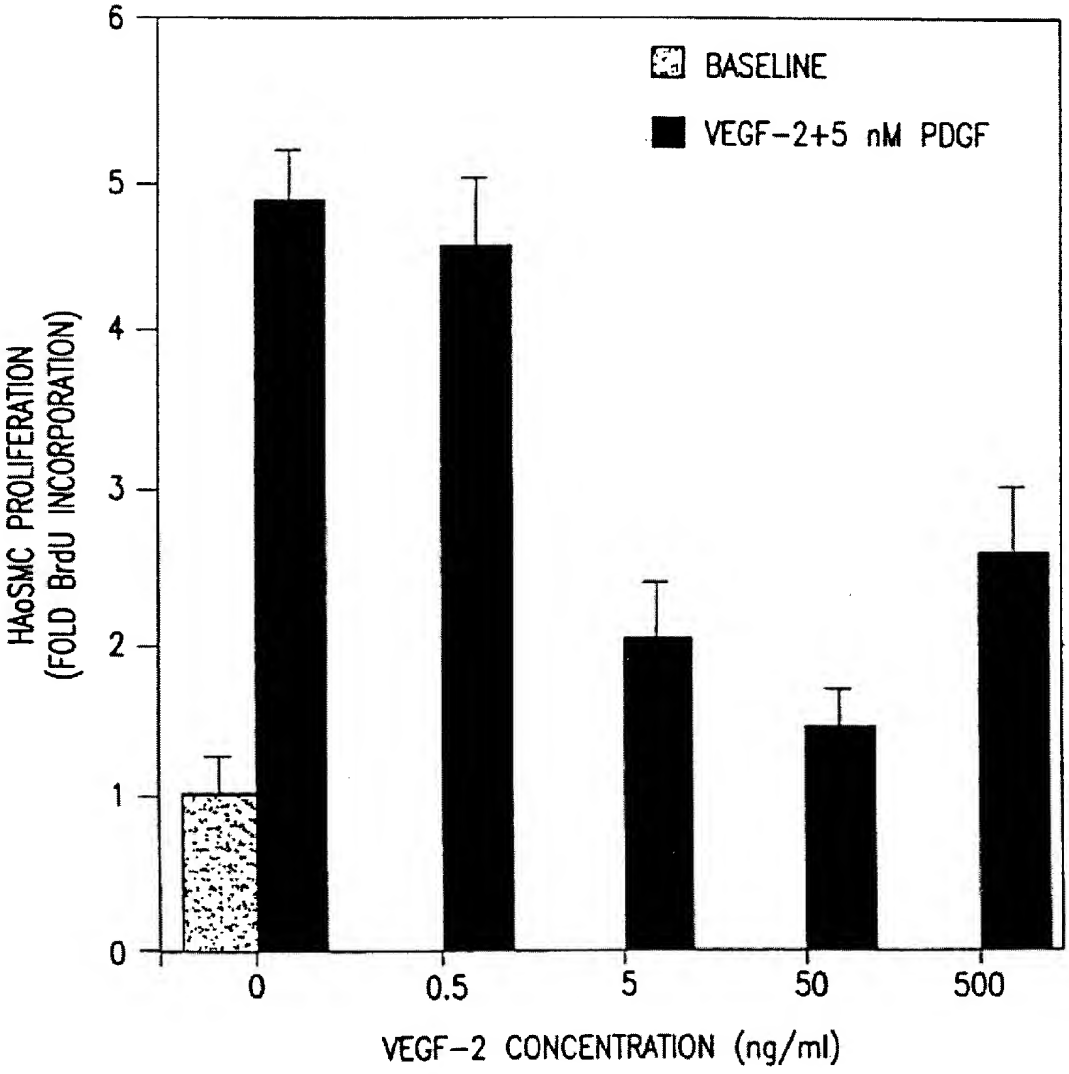


FIG. 20A

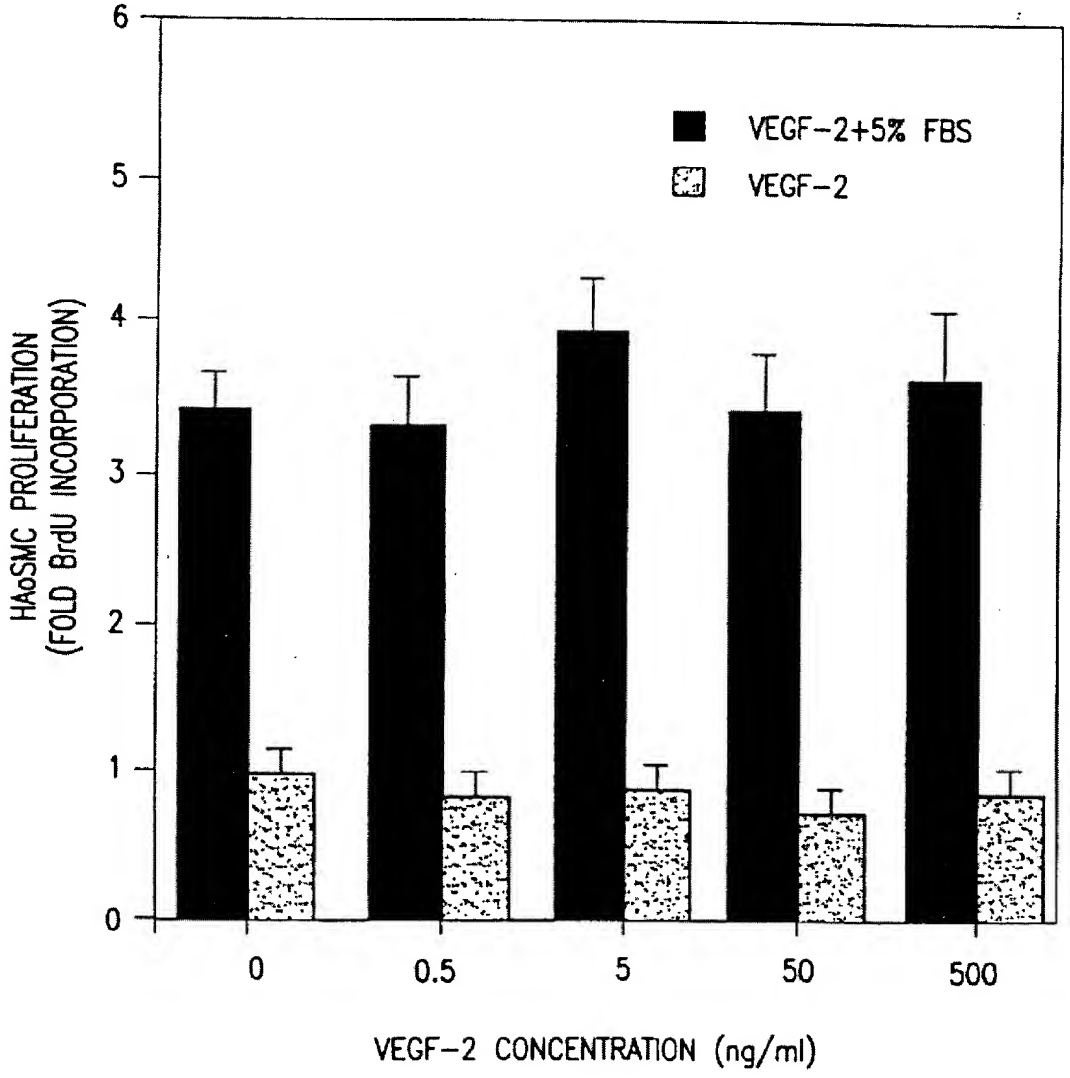


FIG. 20B

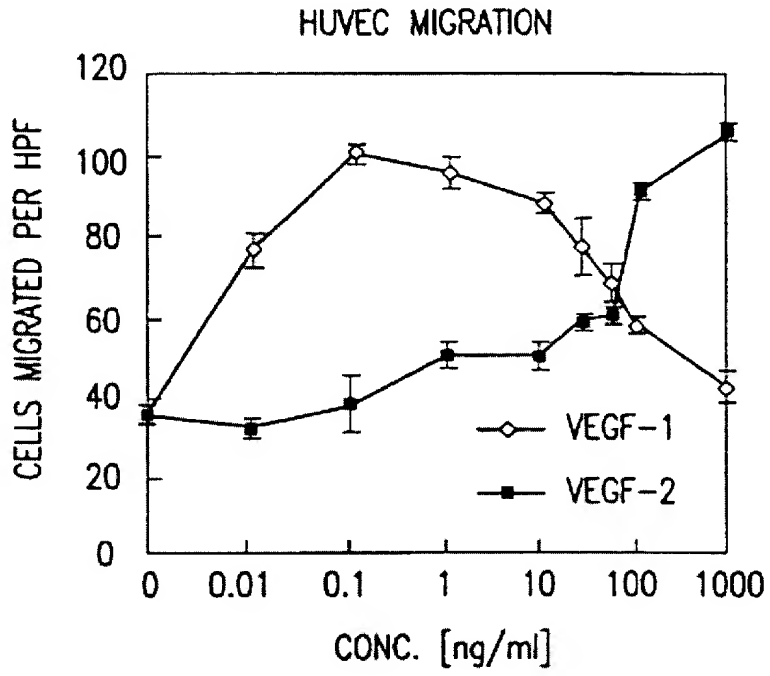


FIG. 21A

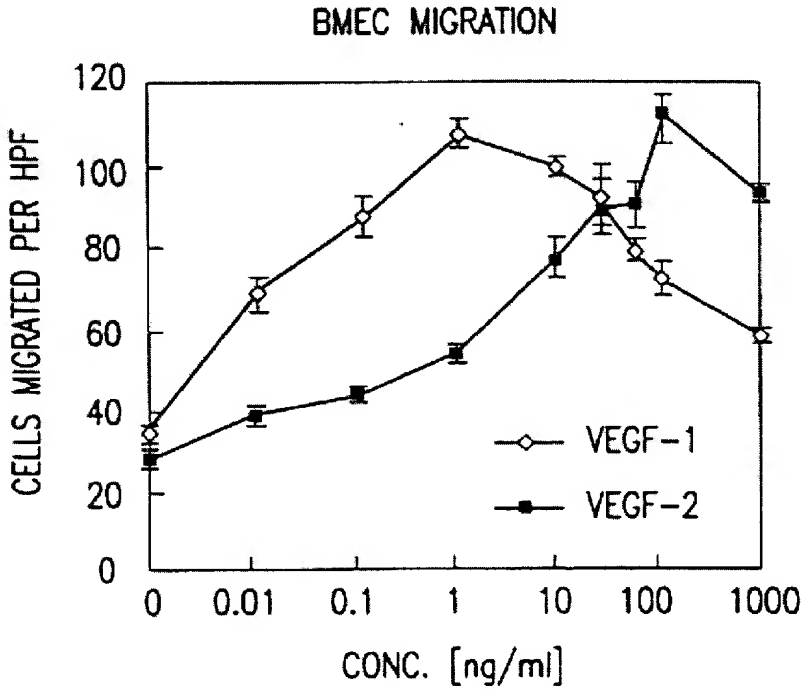


FIG. 21B

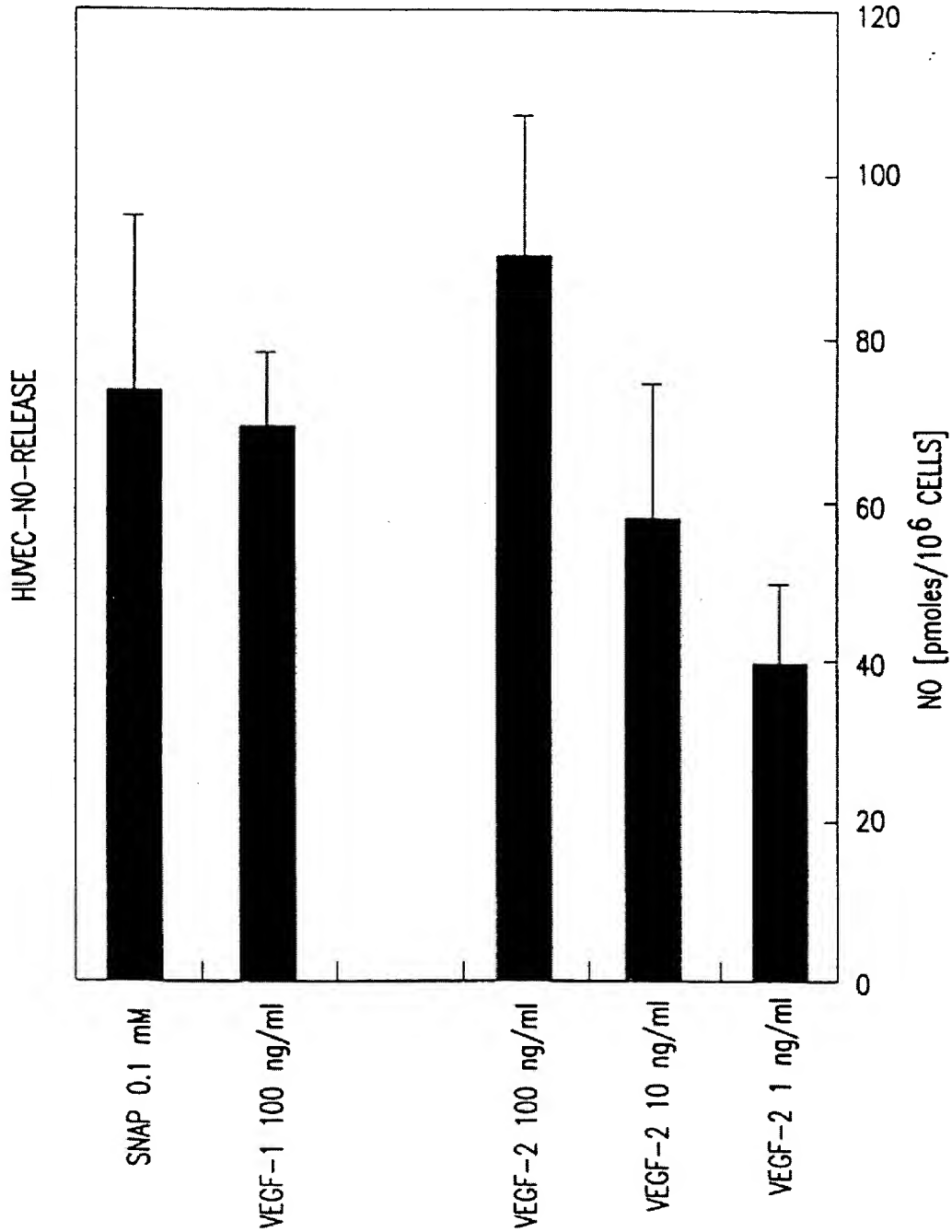


FIG. 22

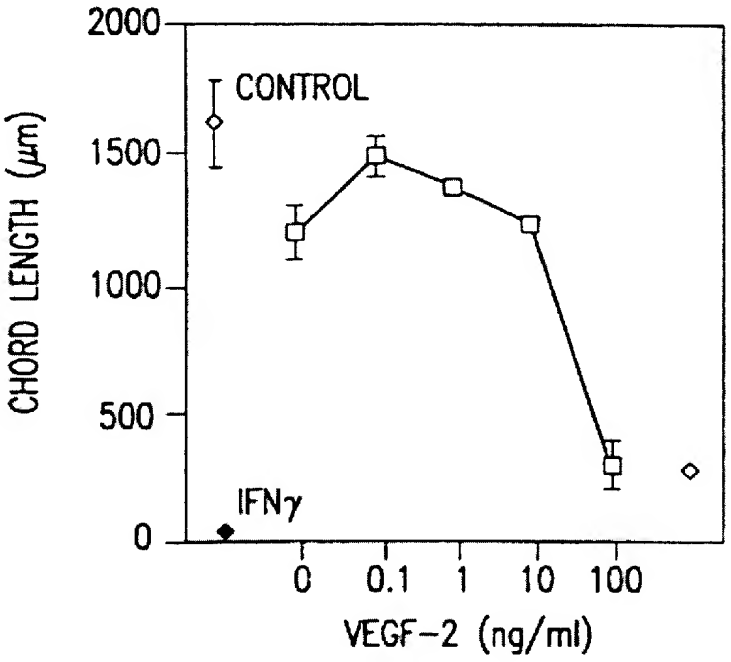


FIG. 23

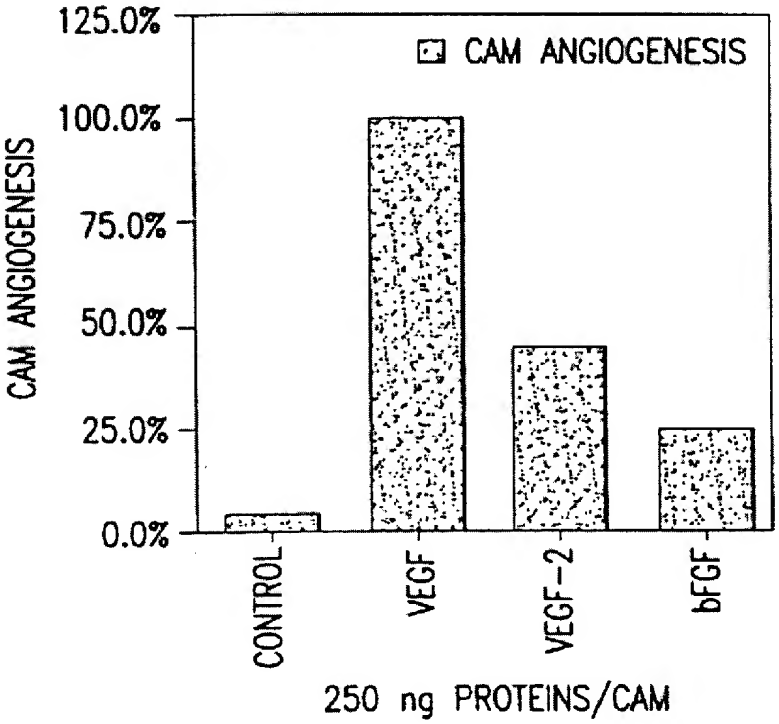


FIG. 24

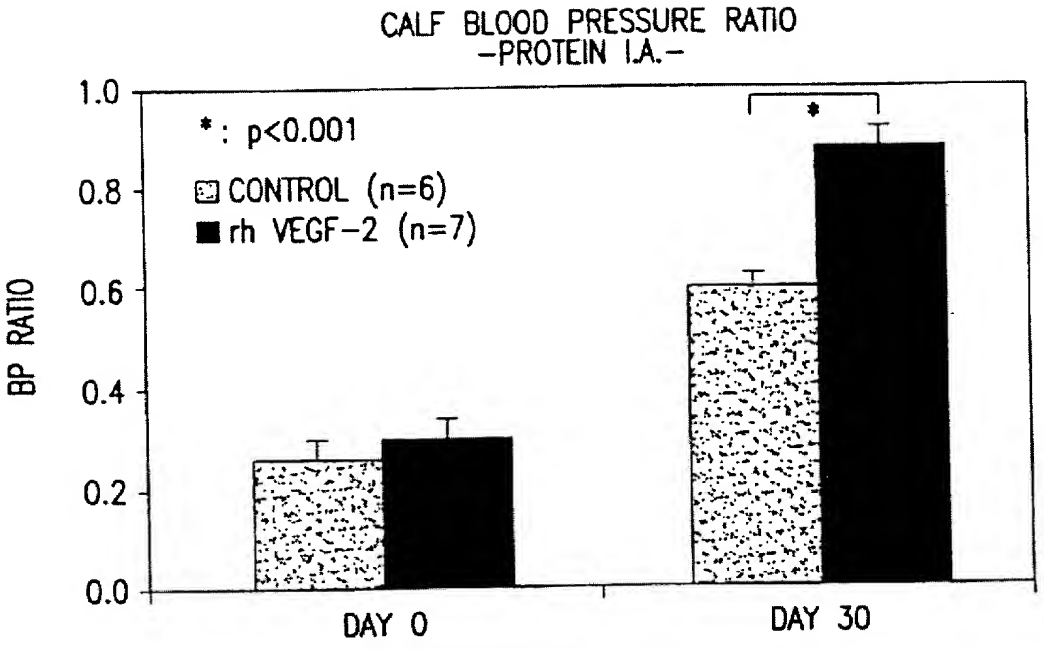


FIG. 25A

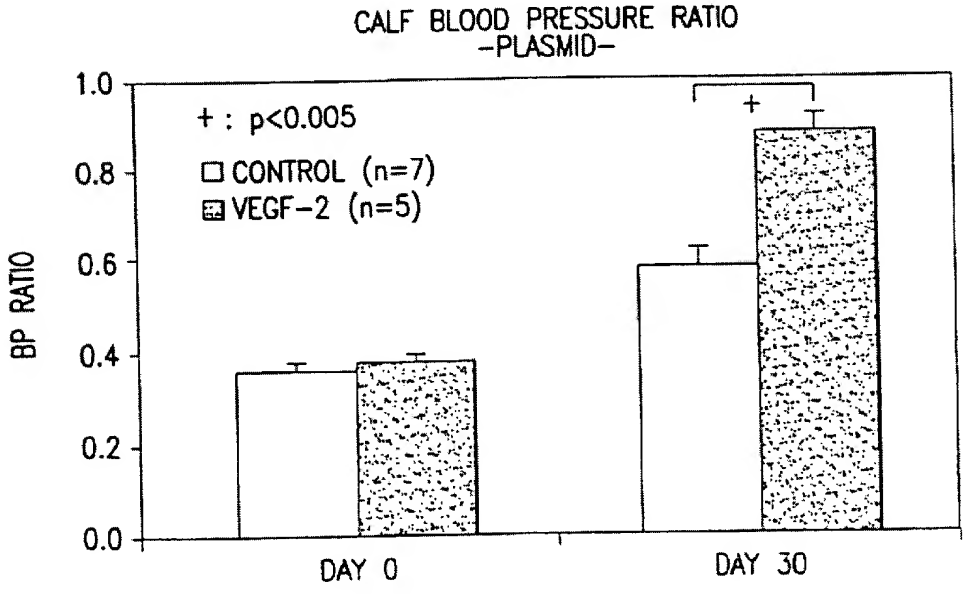


FIG. 25B

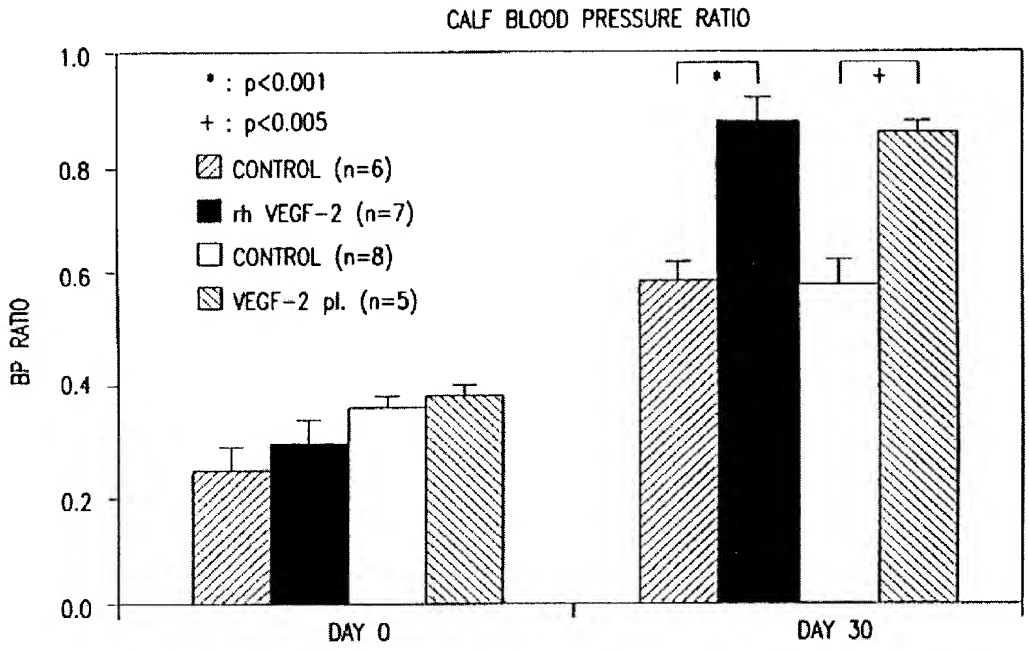


FIG. 25C

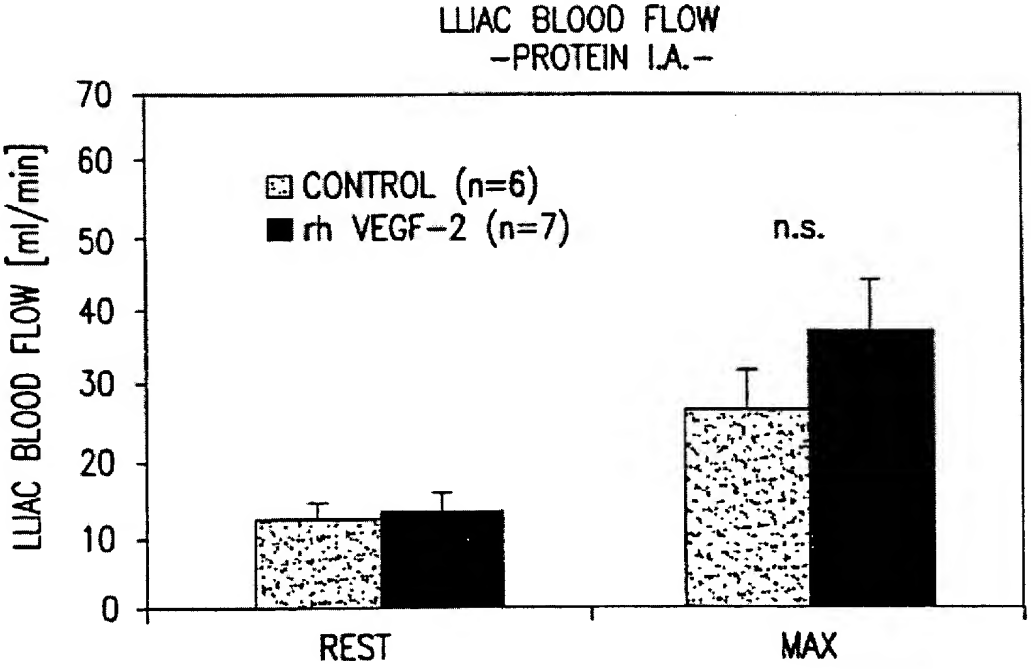


FIG. 25D

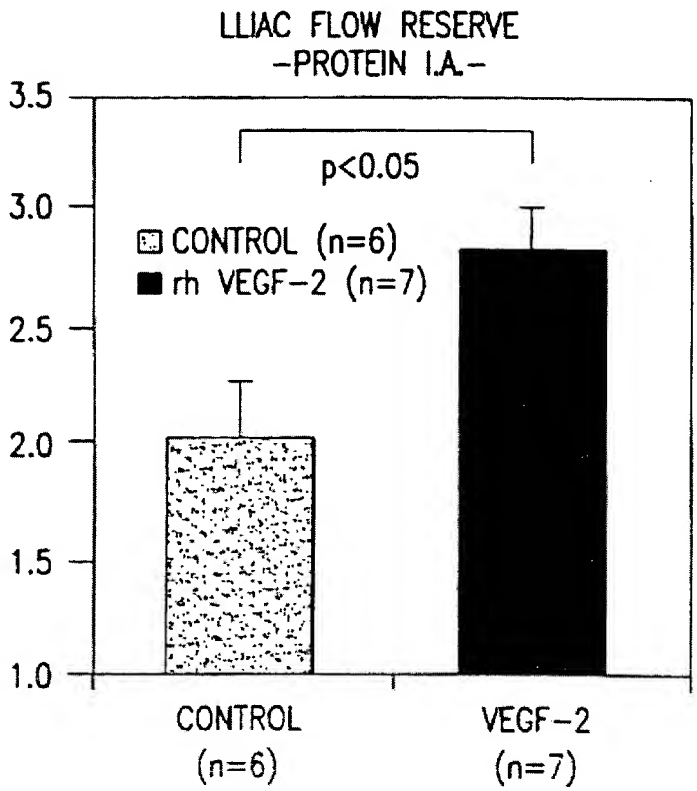


FIG. 25E

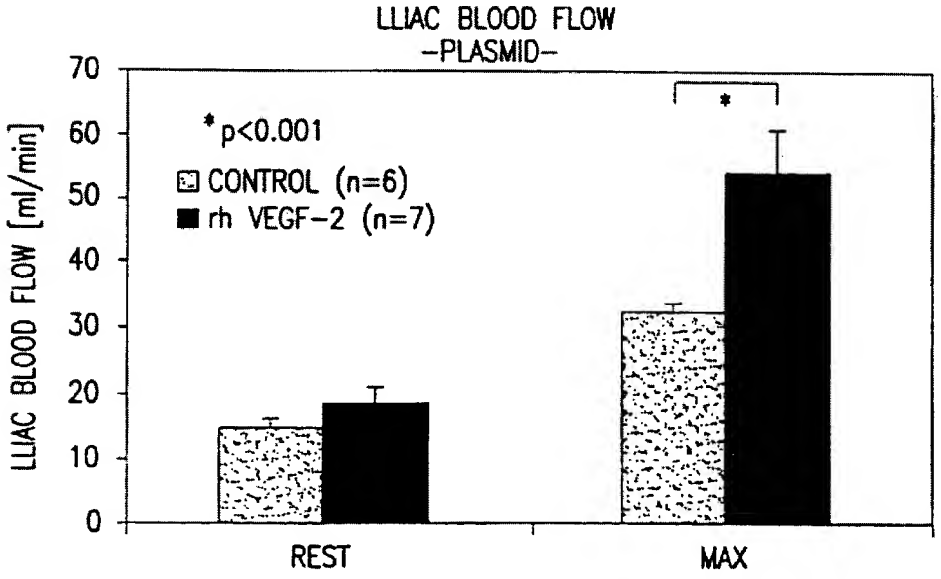


FIG. 25F

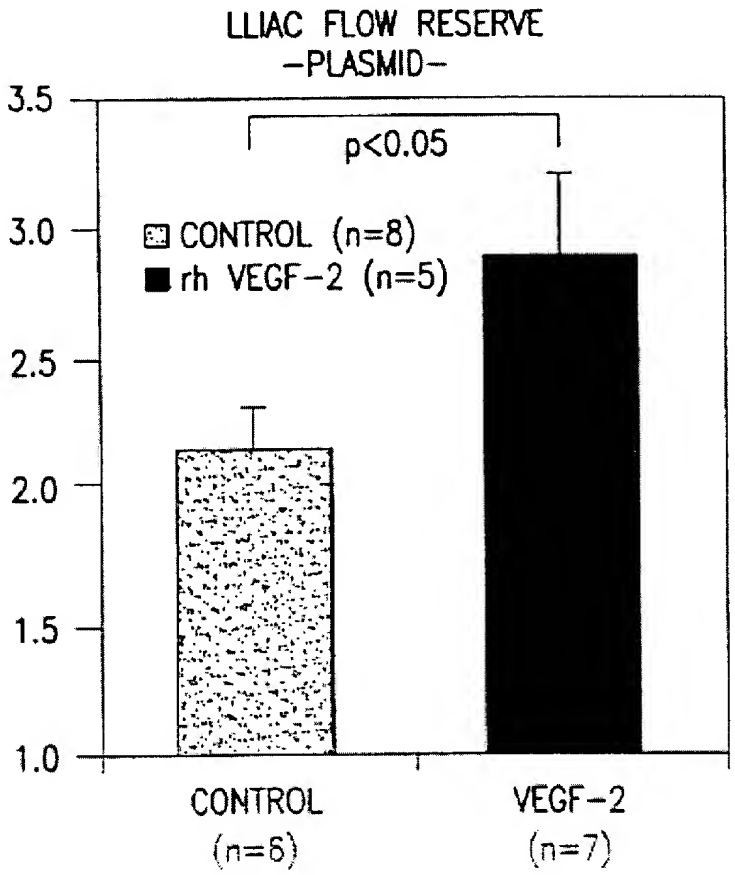


FIG. 25G

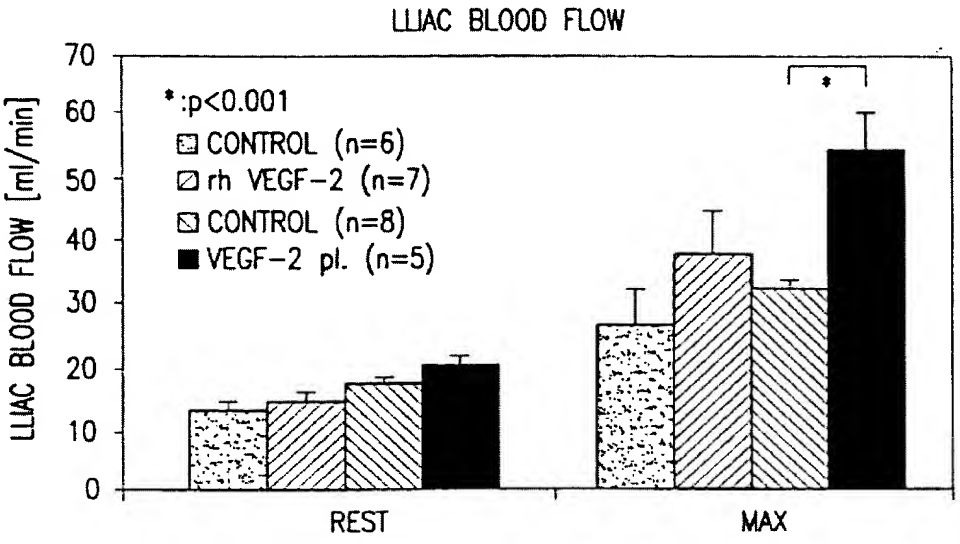


FIG. 25H

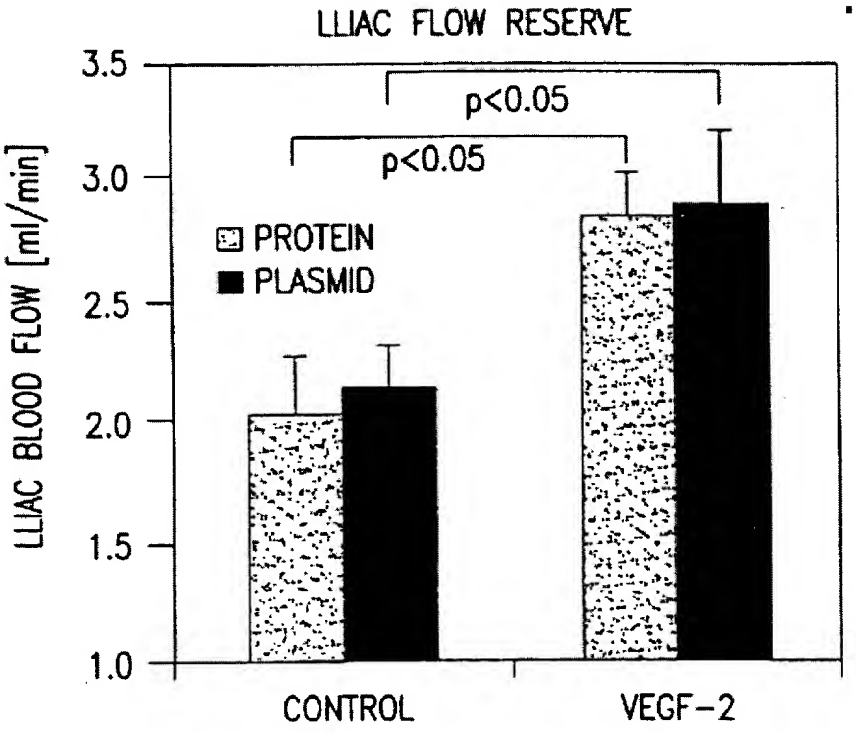


FIG. 25I

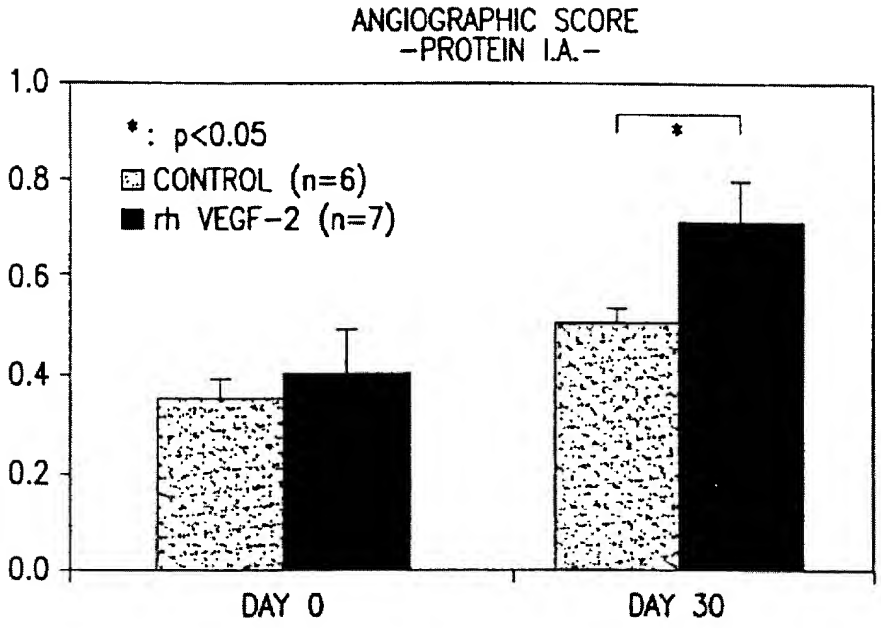


FIG. 25J

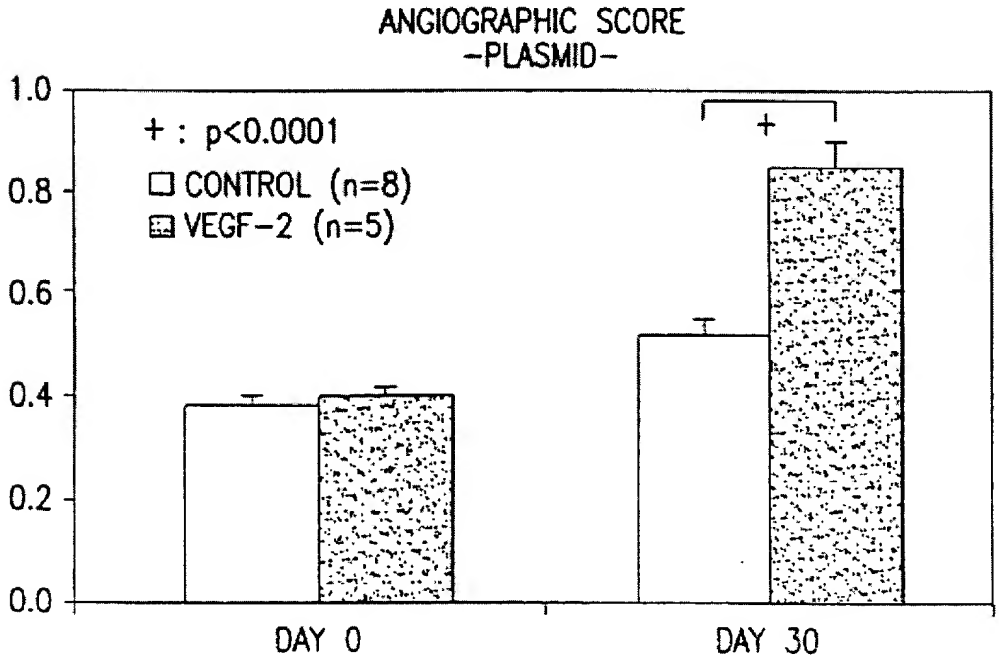


FIG. 25K

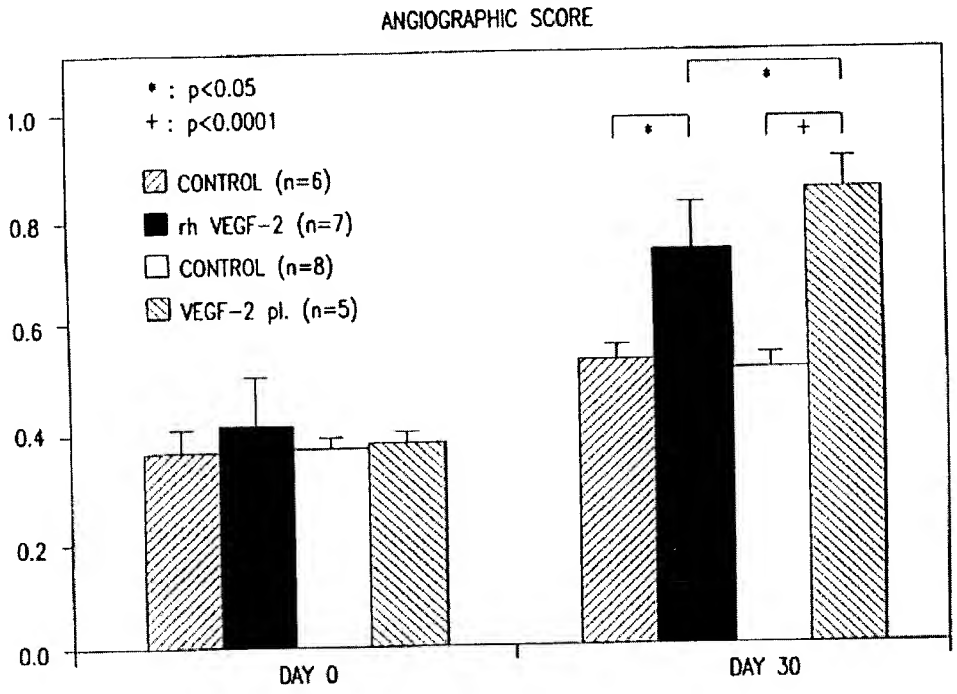


FIG. 25L

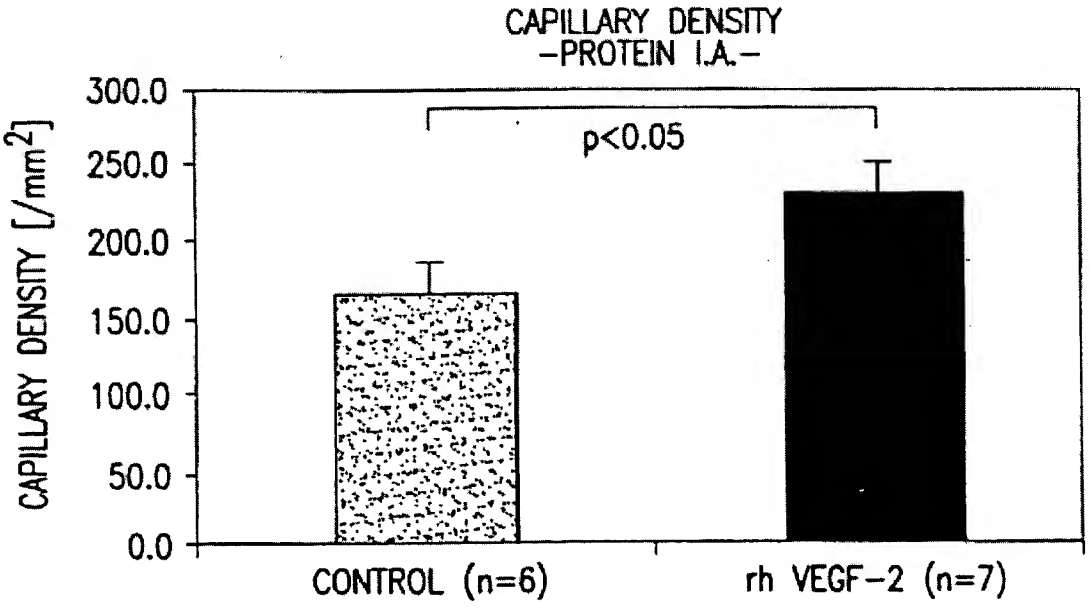


FIG. 25M

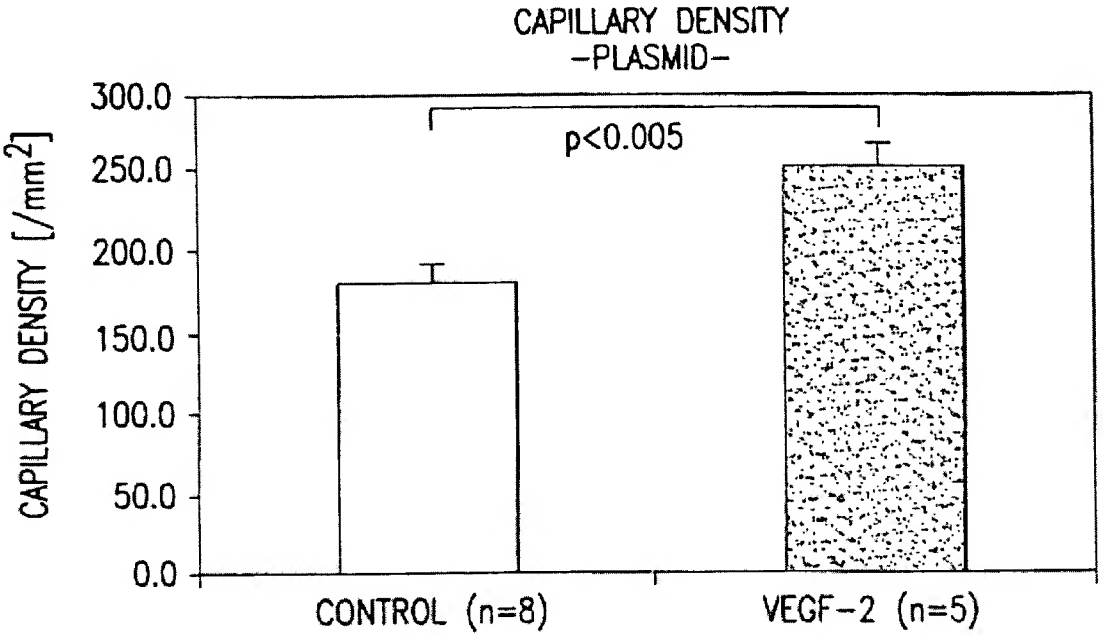


FIG. 25N

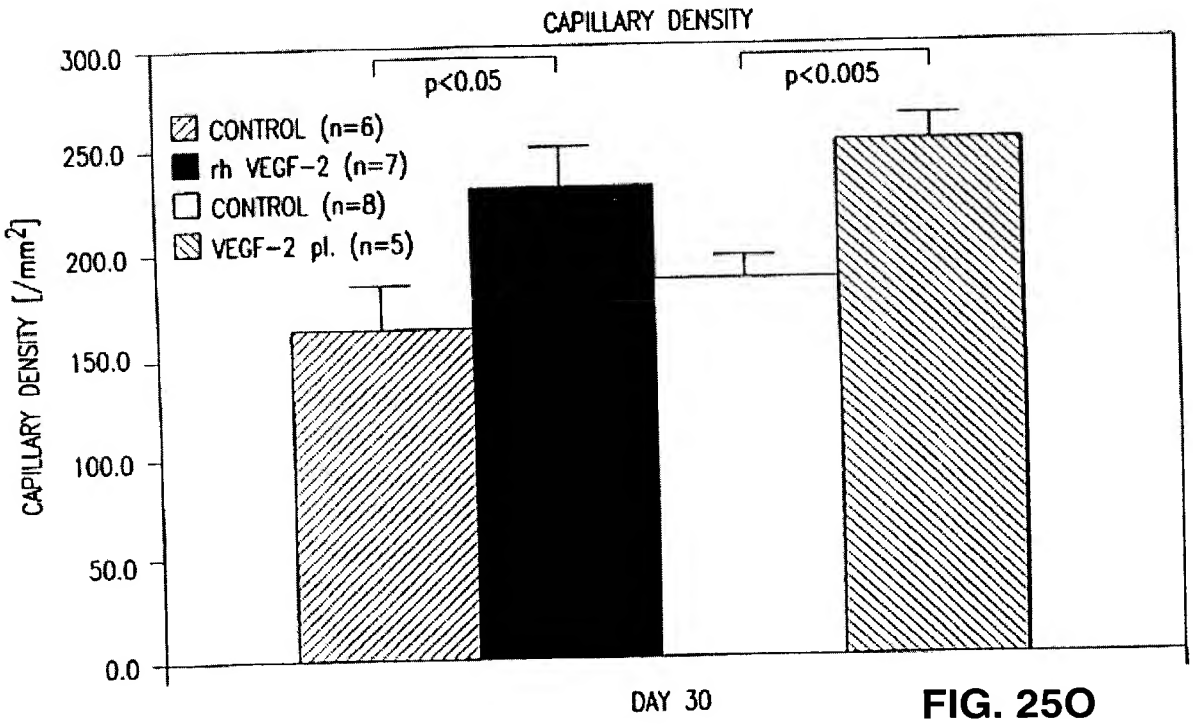


FIG. 25O

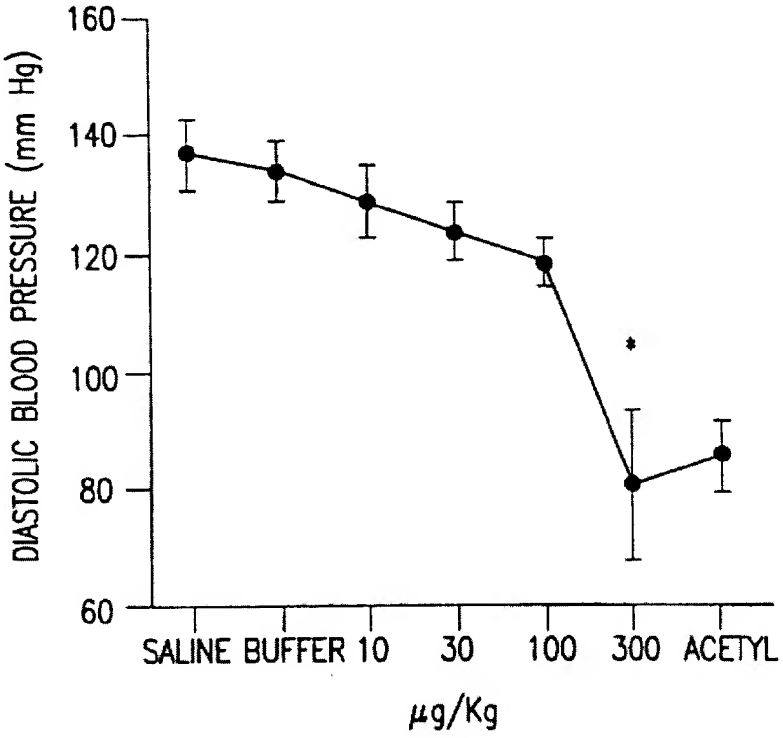


FIG. 26A

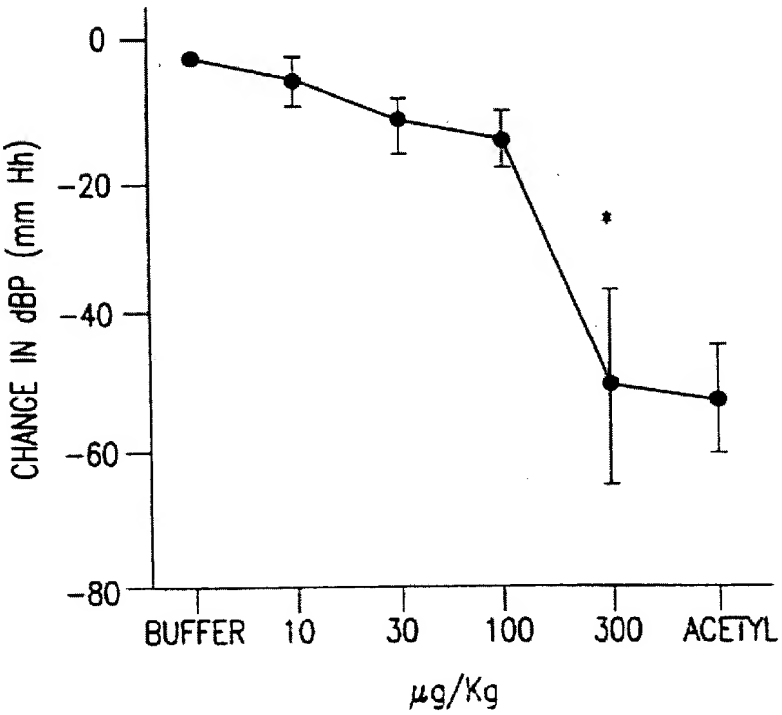


FIG. 26B

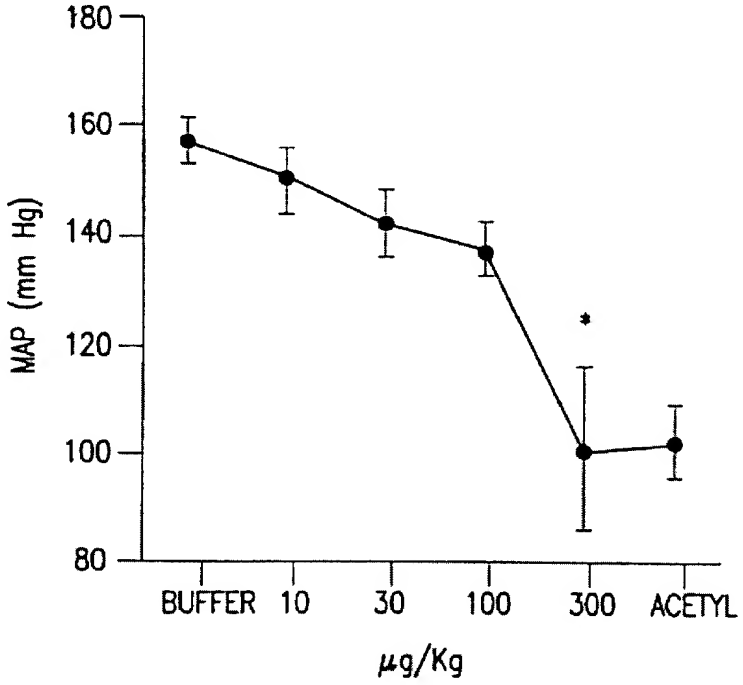


FIG. 26C

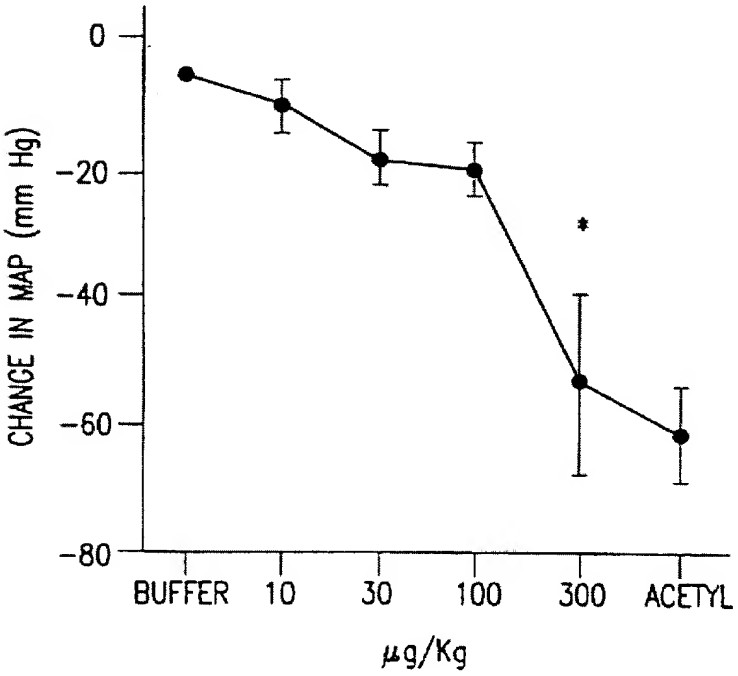


FIG. 26D

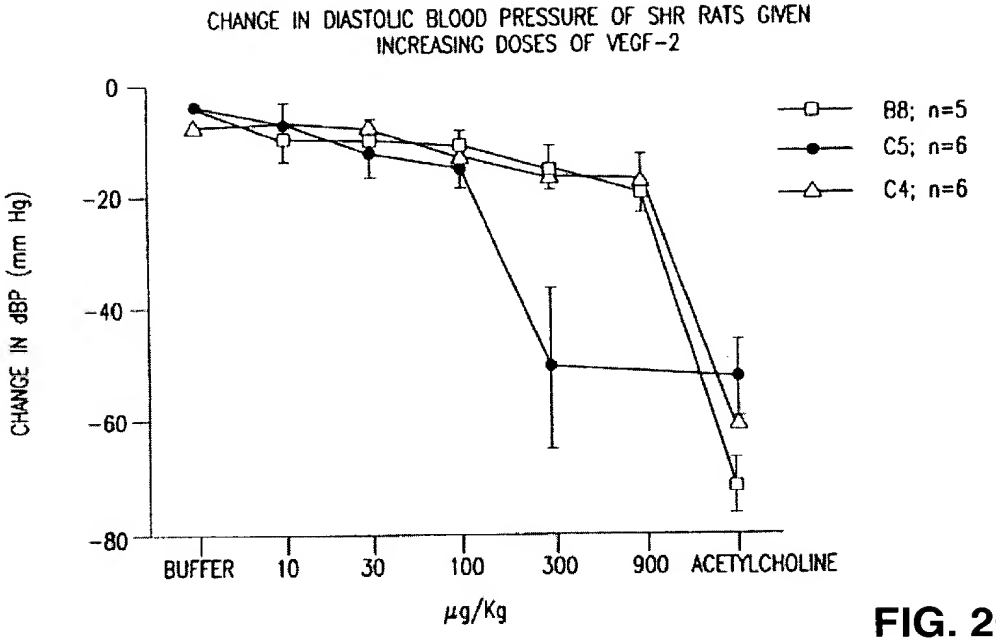


FIG. 26E

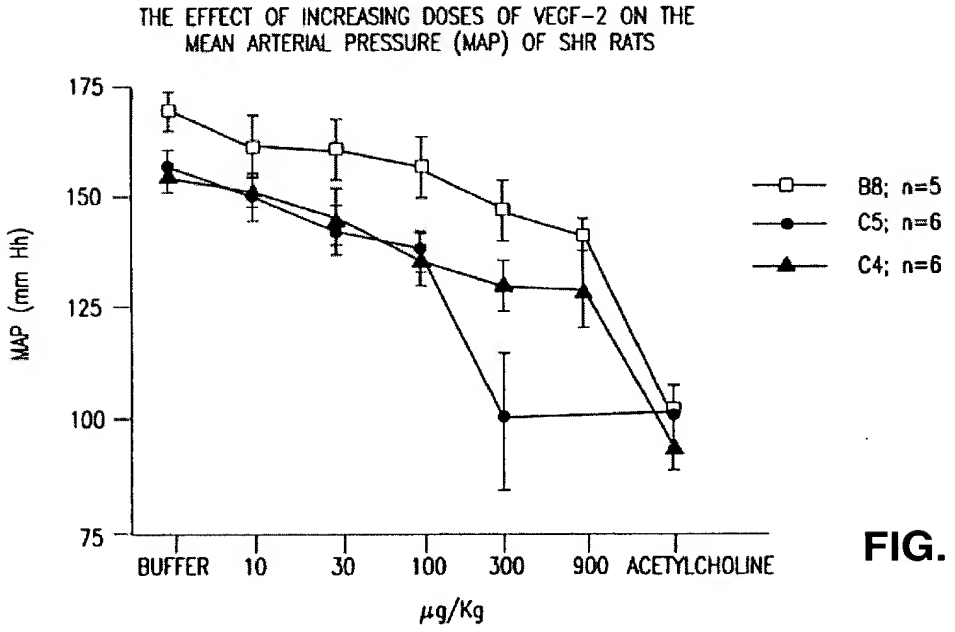


FIG. 26F

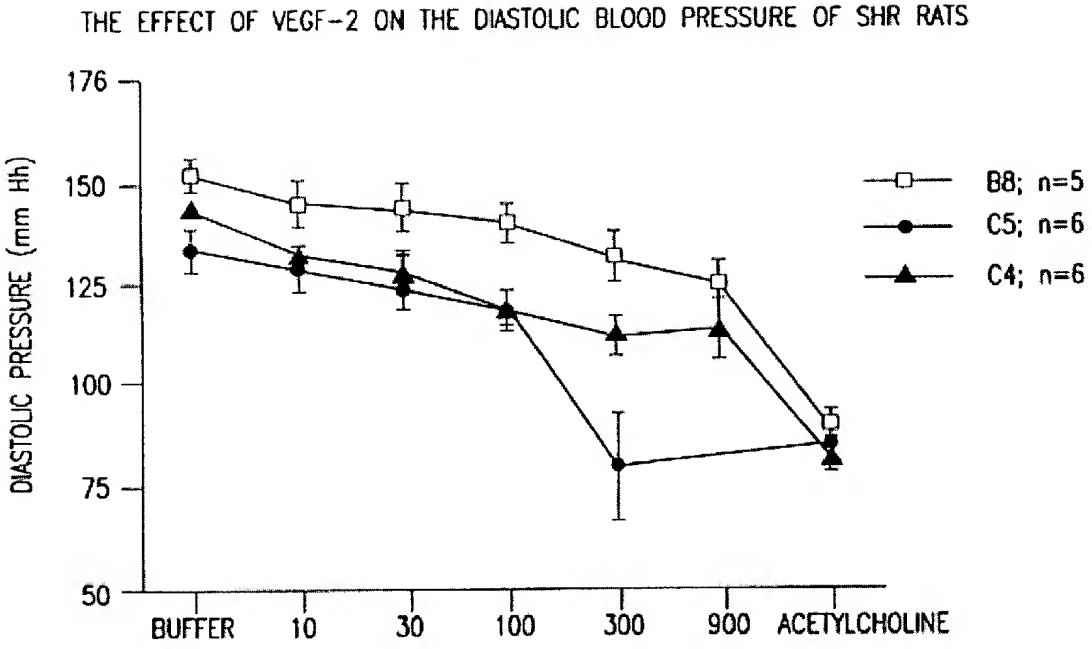


FIG. 26G

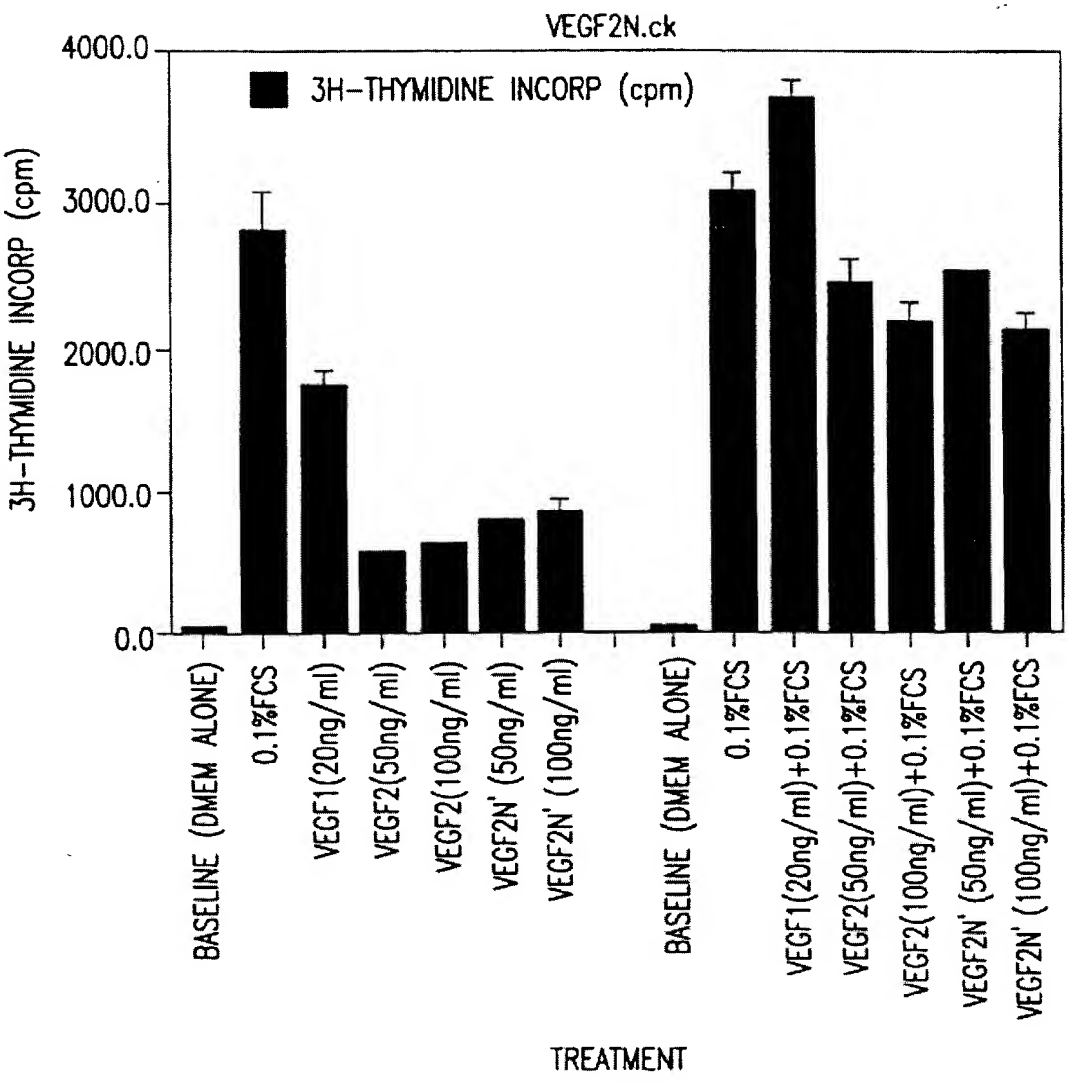


FIG. 27

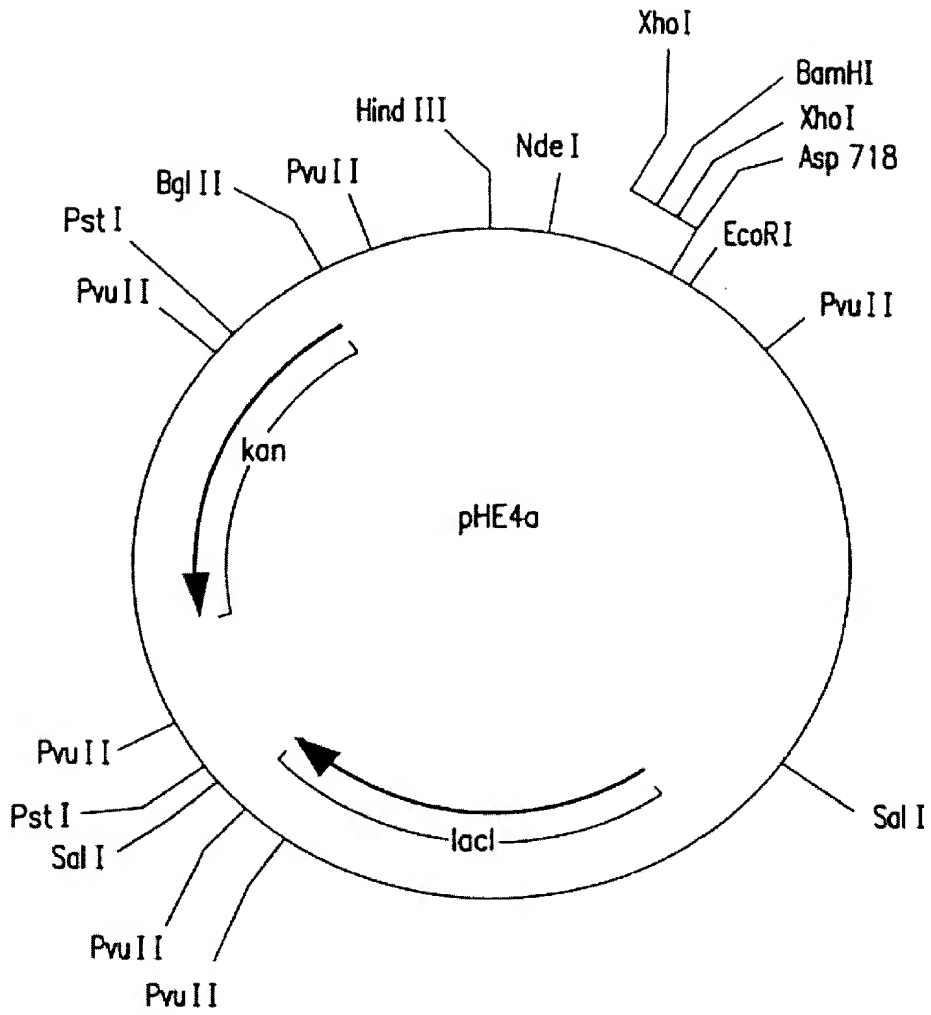


FIG. 28

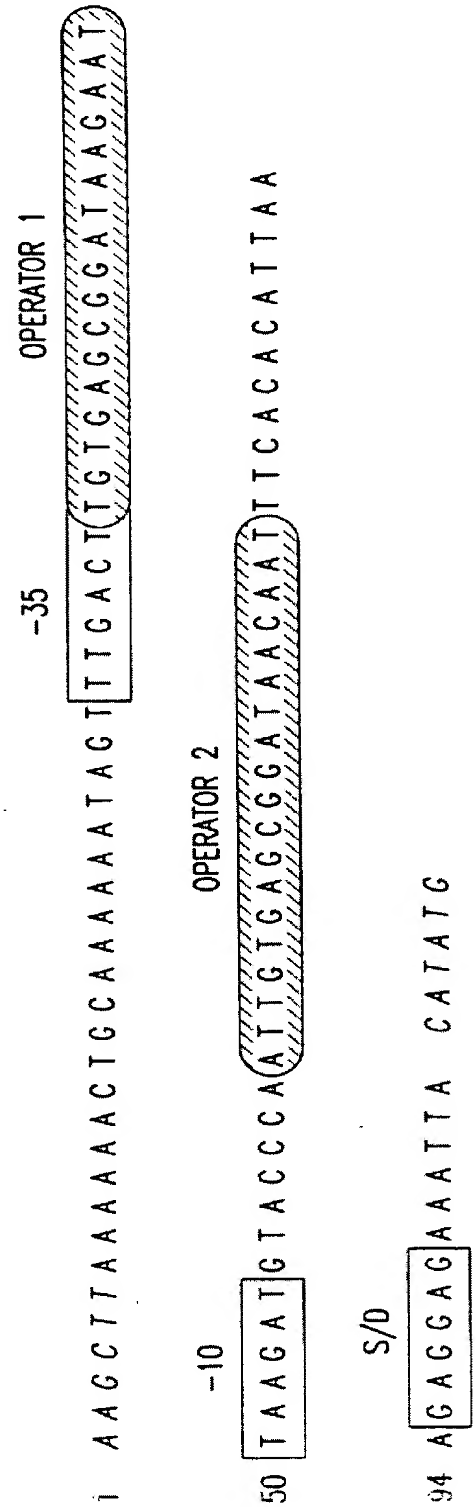

OPERATOR 1
-35
1 AAGCTTAAAAAACTGCAAAAAATAGTTTGACTTGTGAGCGGATAAGAAT
-10
OPERATOR 2
50 TAAGATGTACCCAATTGTGAGCGGATAACAATTTCACACATTAA
S/D
94 AGAGGAGAAATTA CATATG

FIG. 29

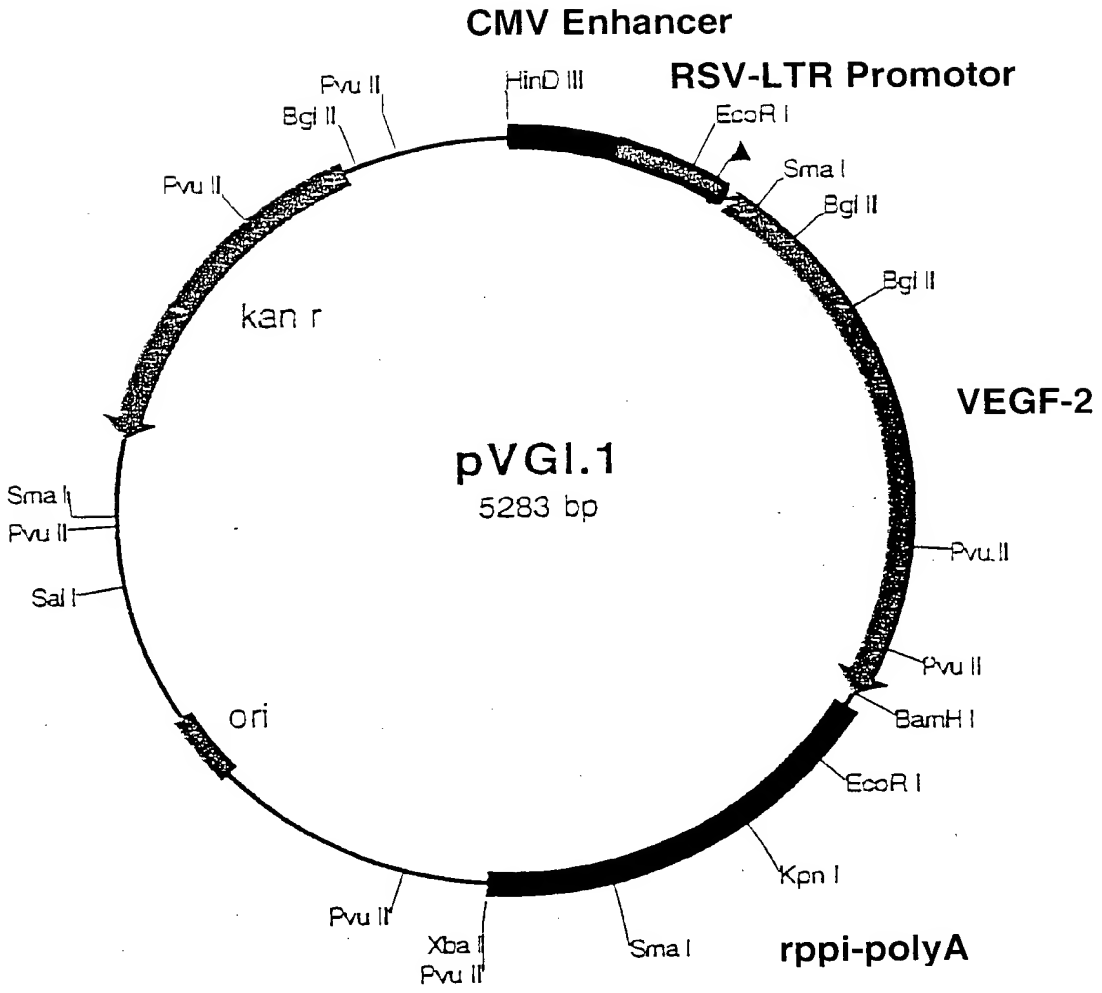


FIG. 30

FIG.31A

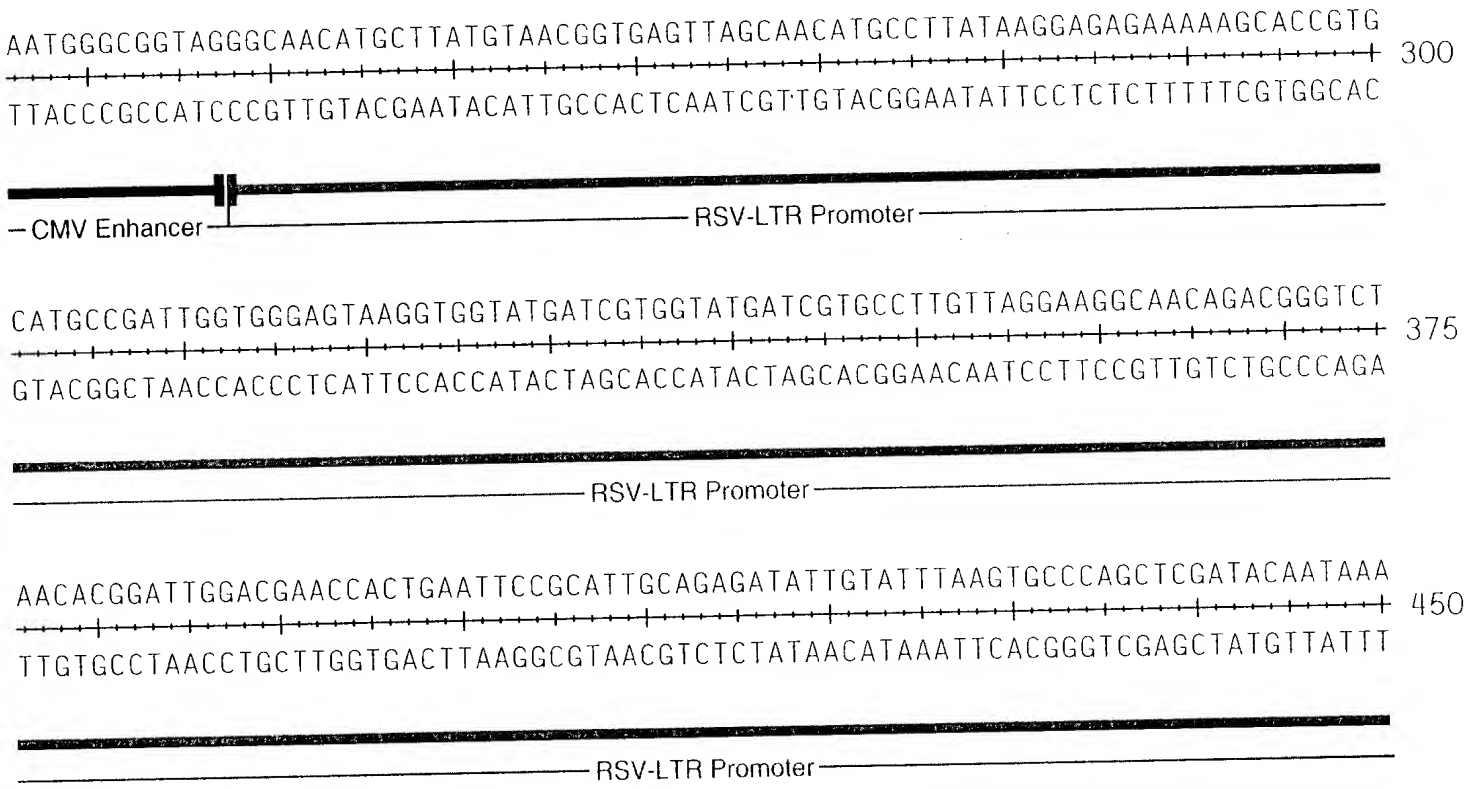


FIG.31B

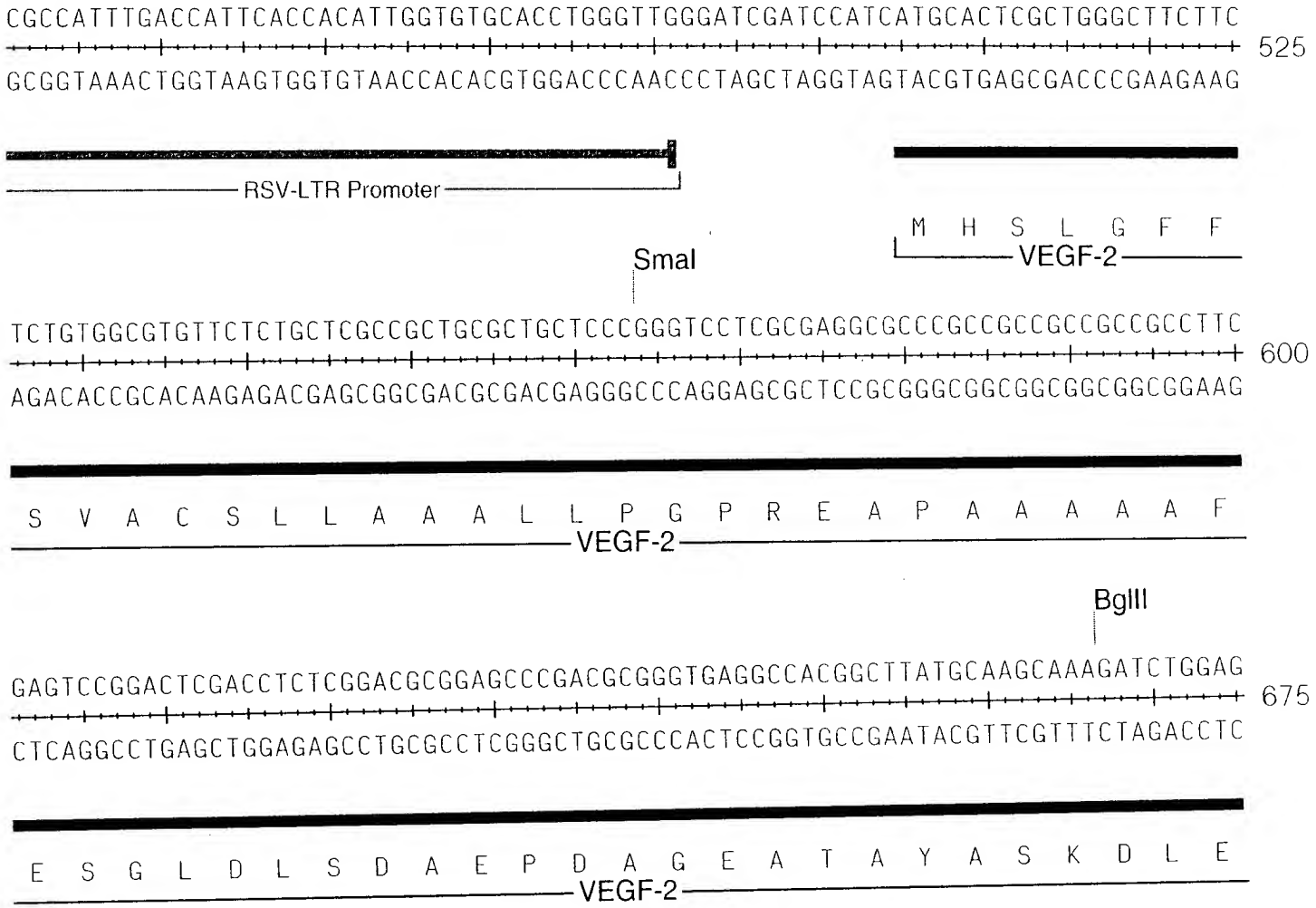


FIG.31C

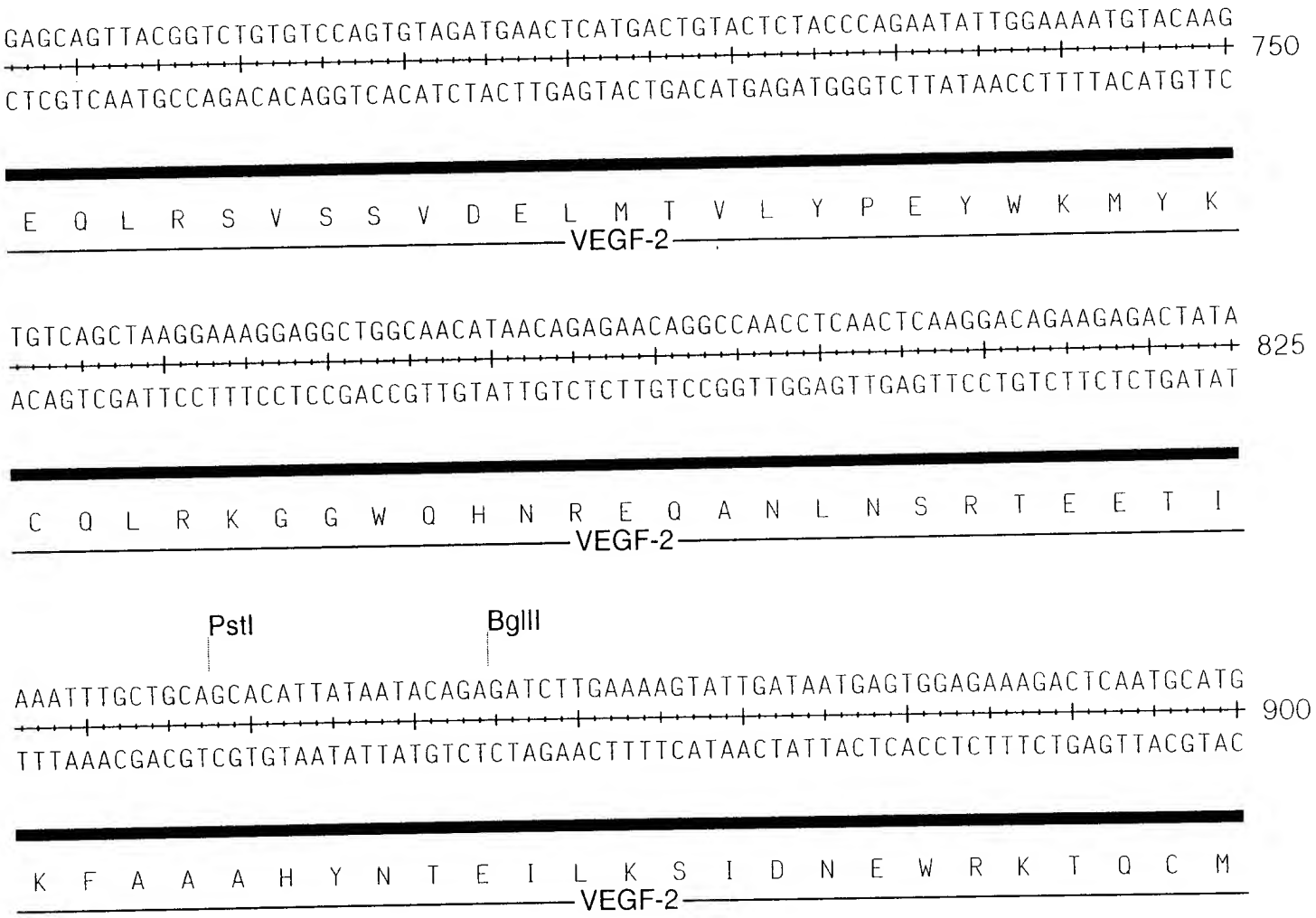


FIG.31D

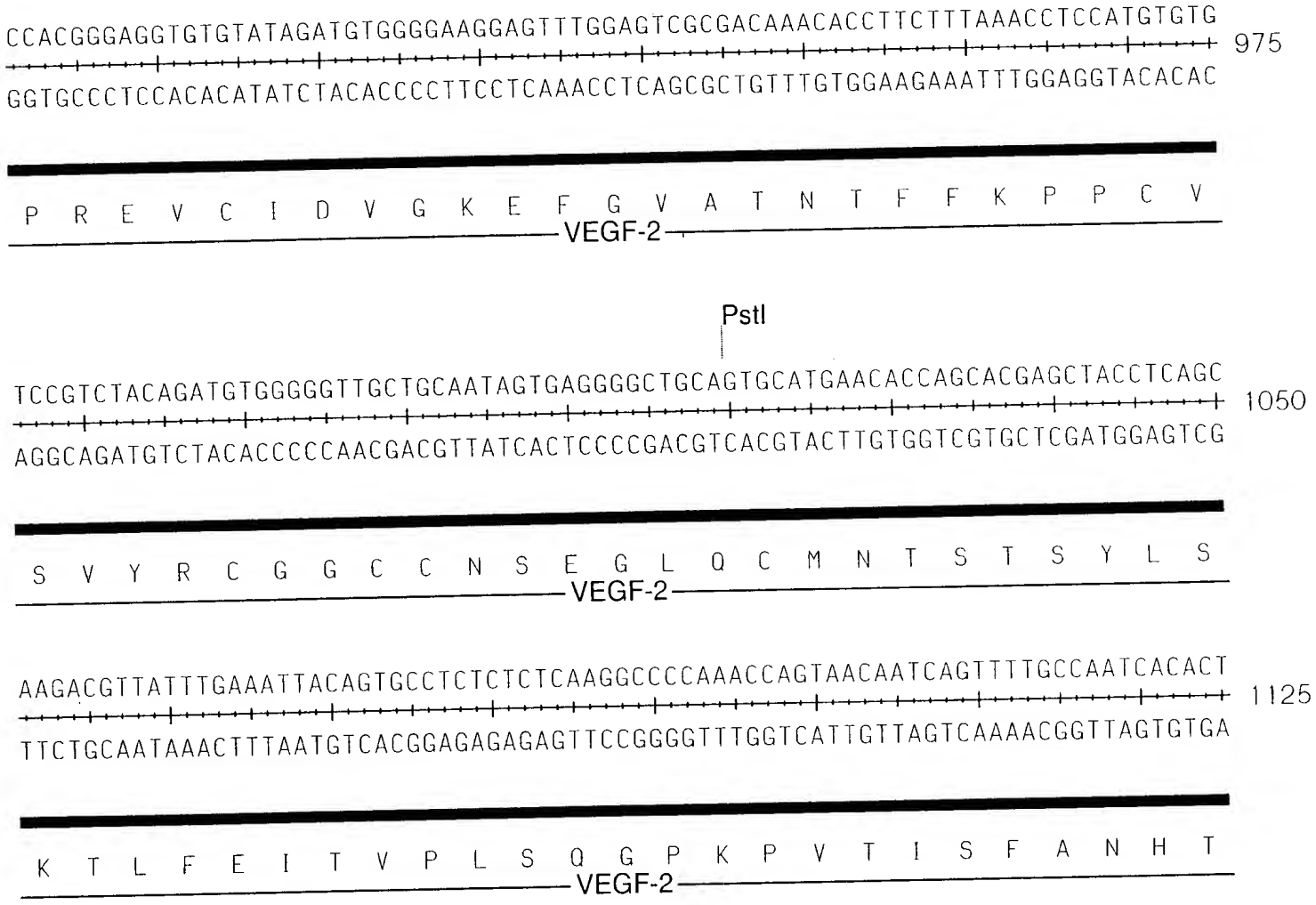


FIG.31E

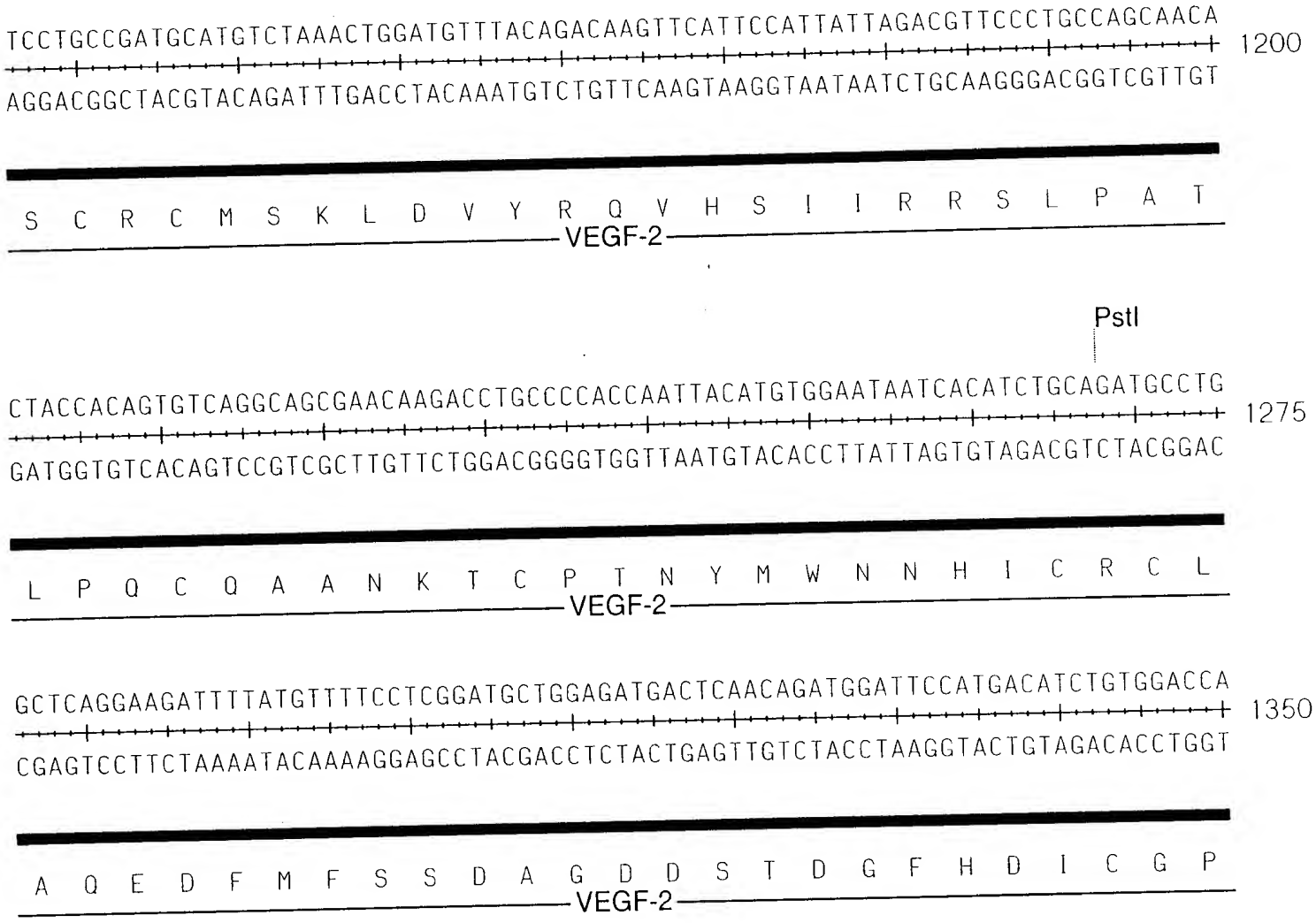


FIG.31F

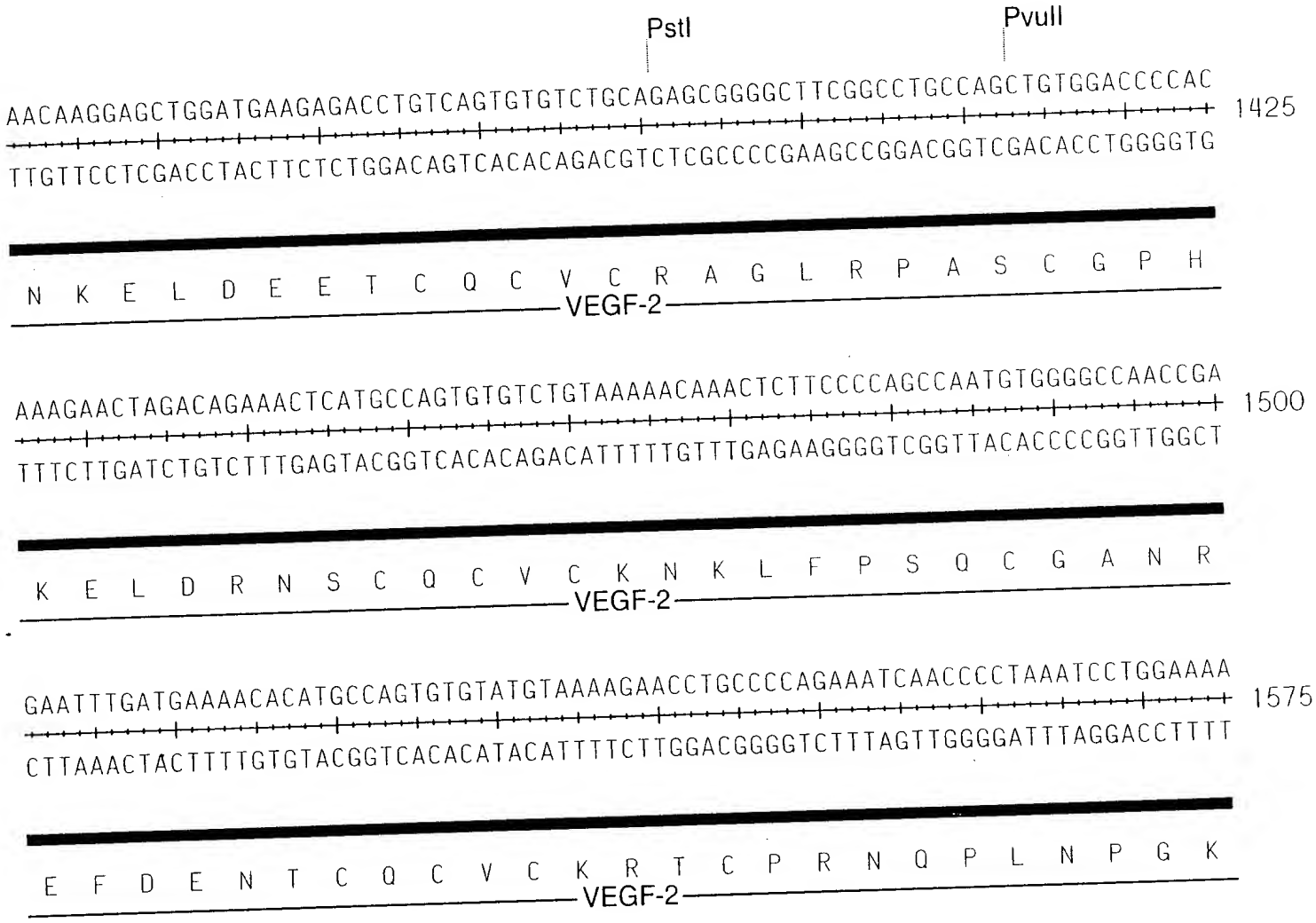


FIG.31G

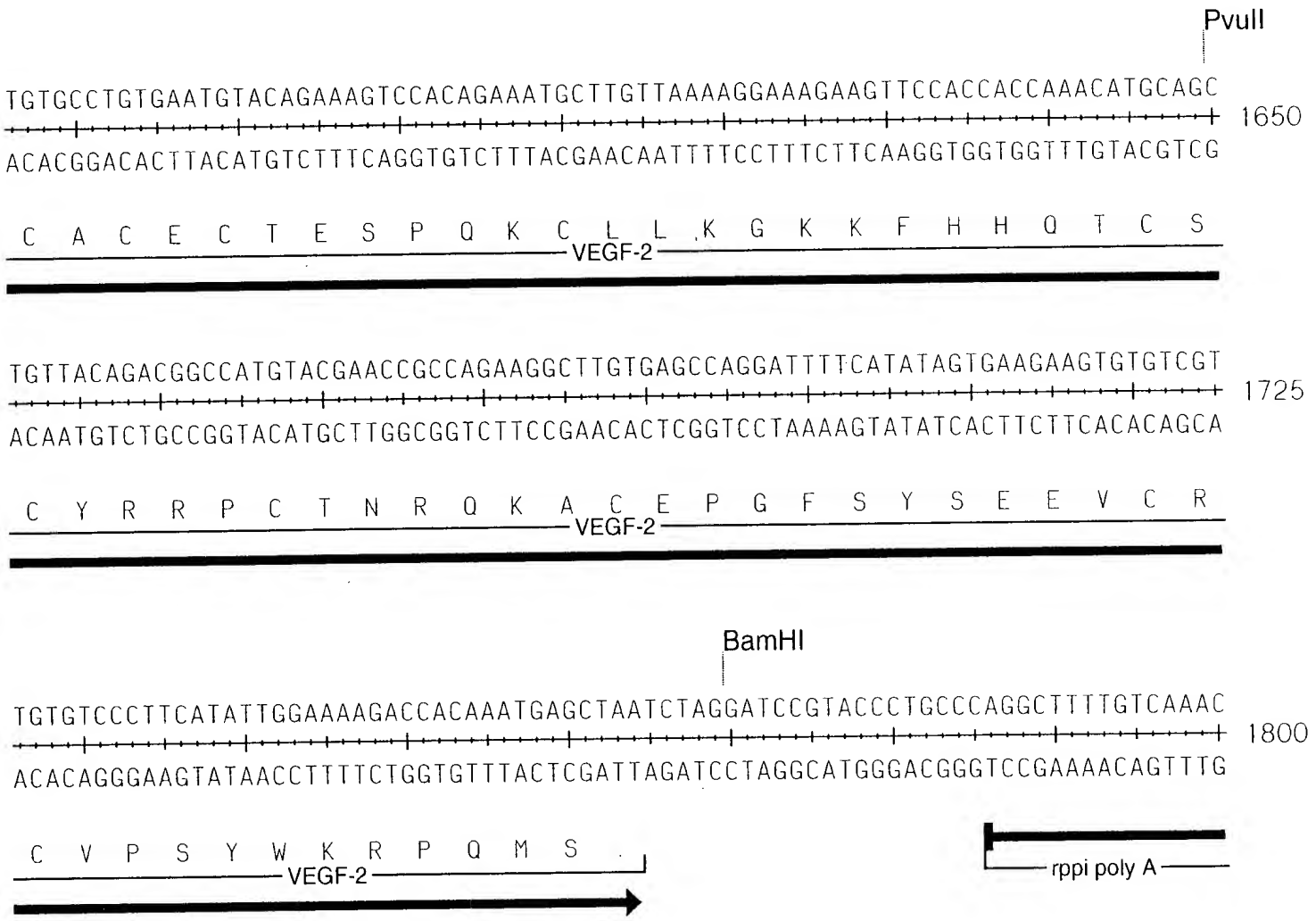


FIG.31H

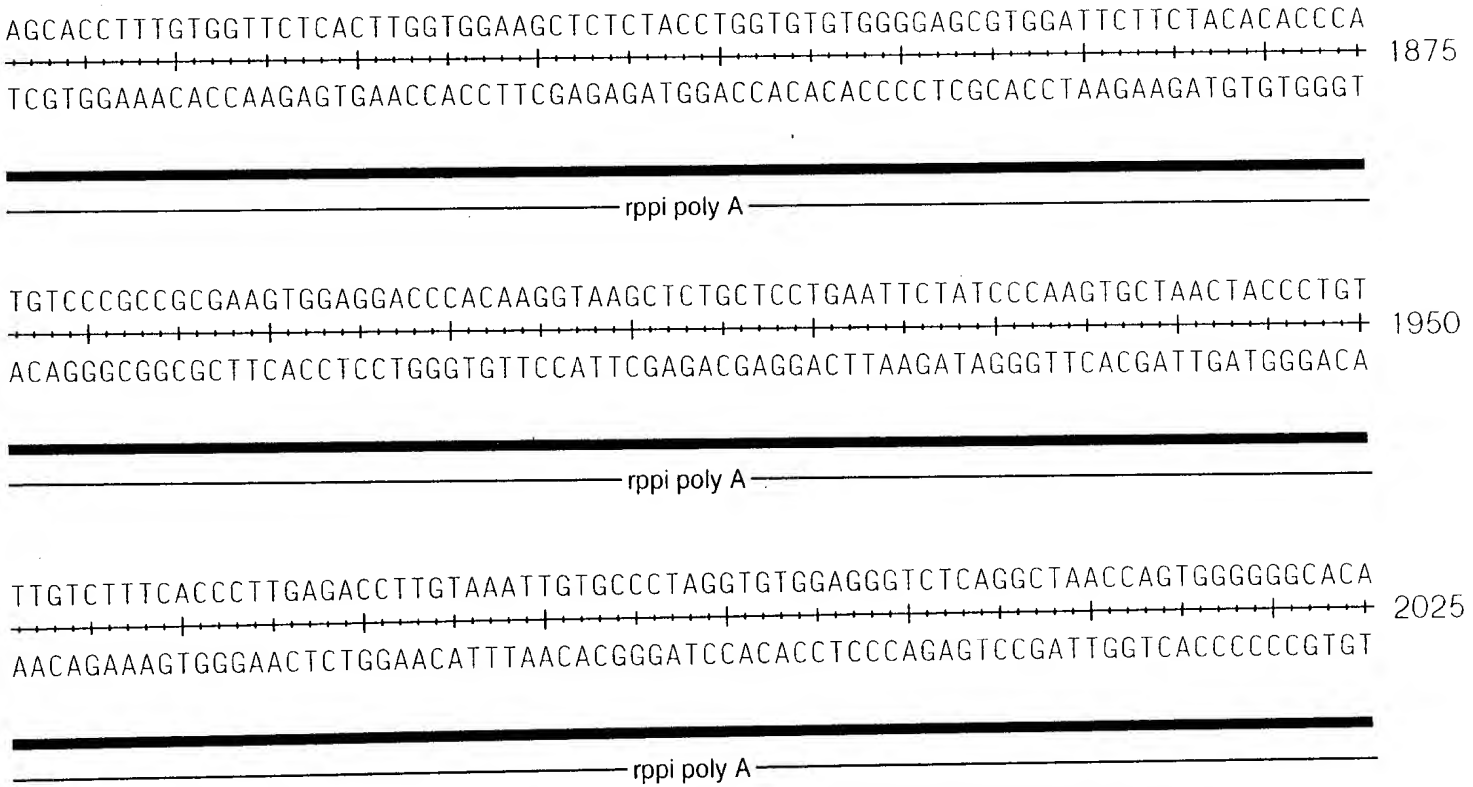


FIG.31I

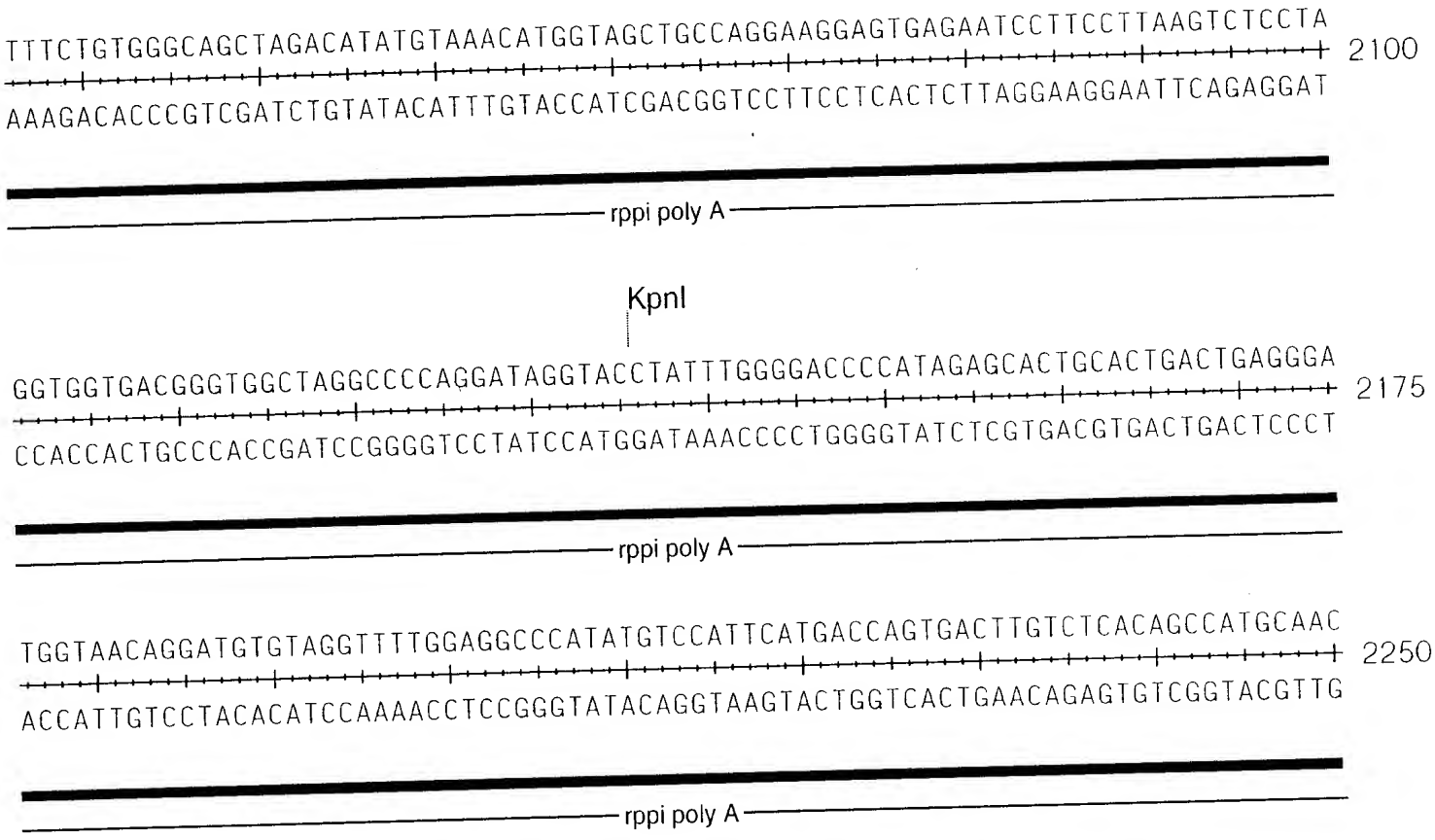


FIG.31J

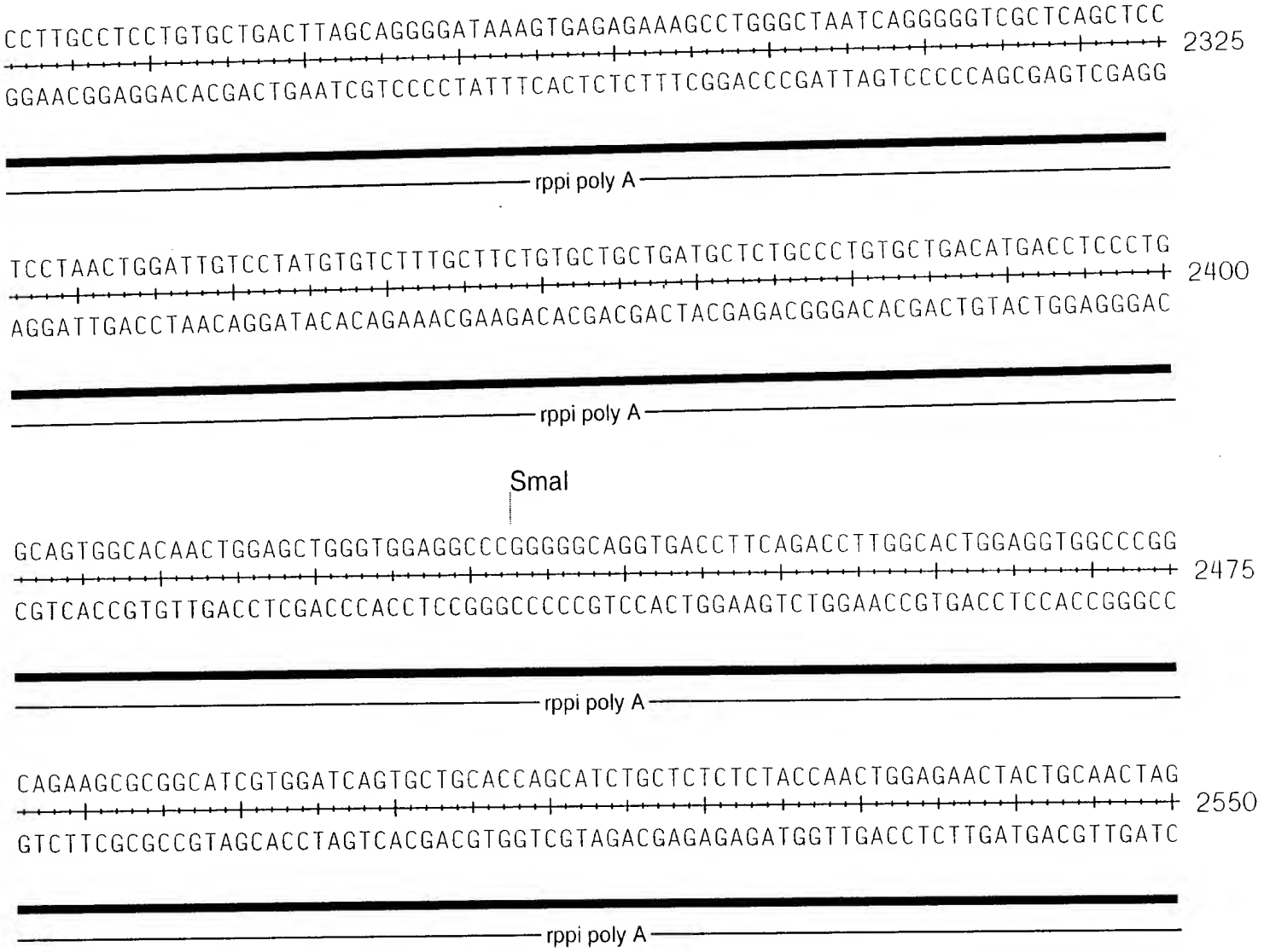


FIG.31K

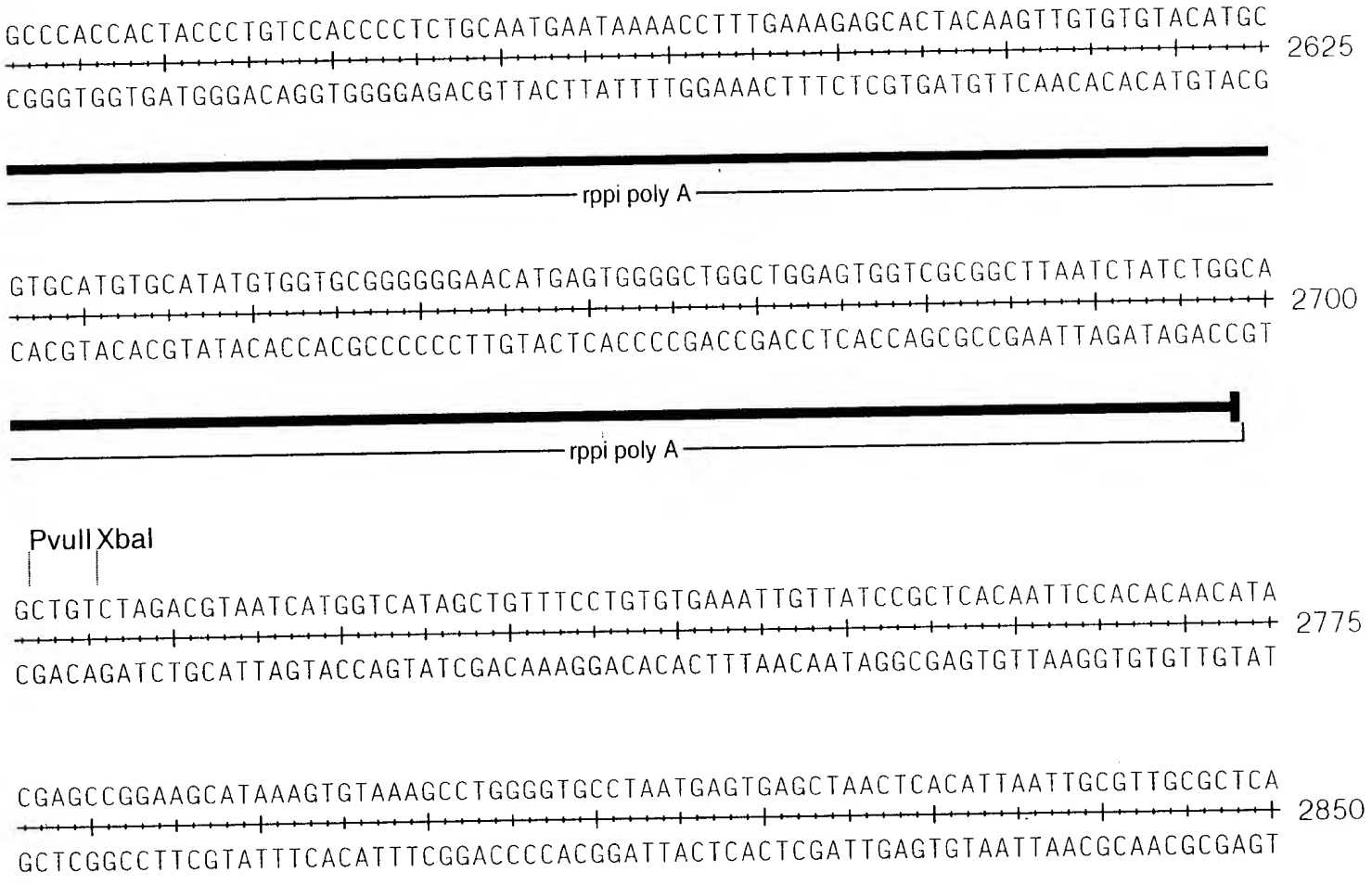


FIG.31L

FIG.31M

FIG.31N

FIG.31O

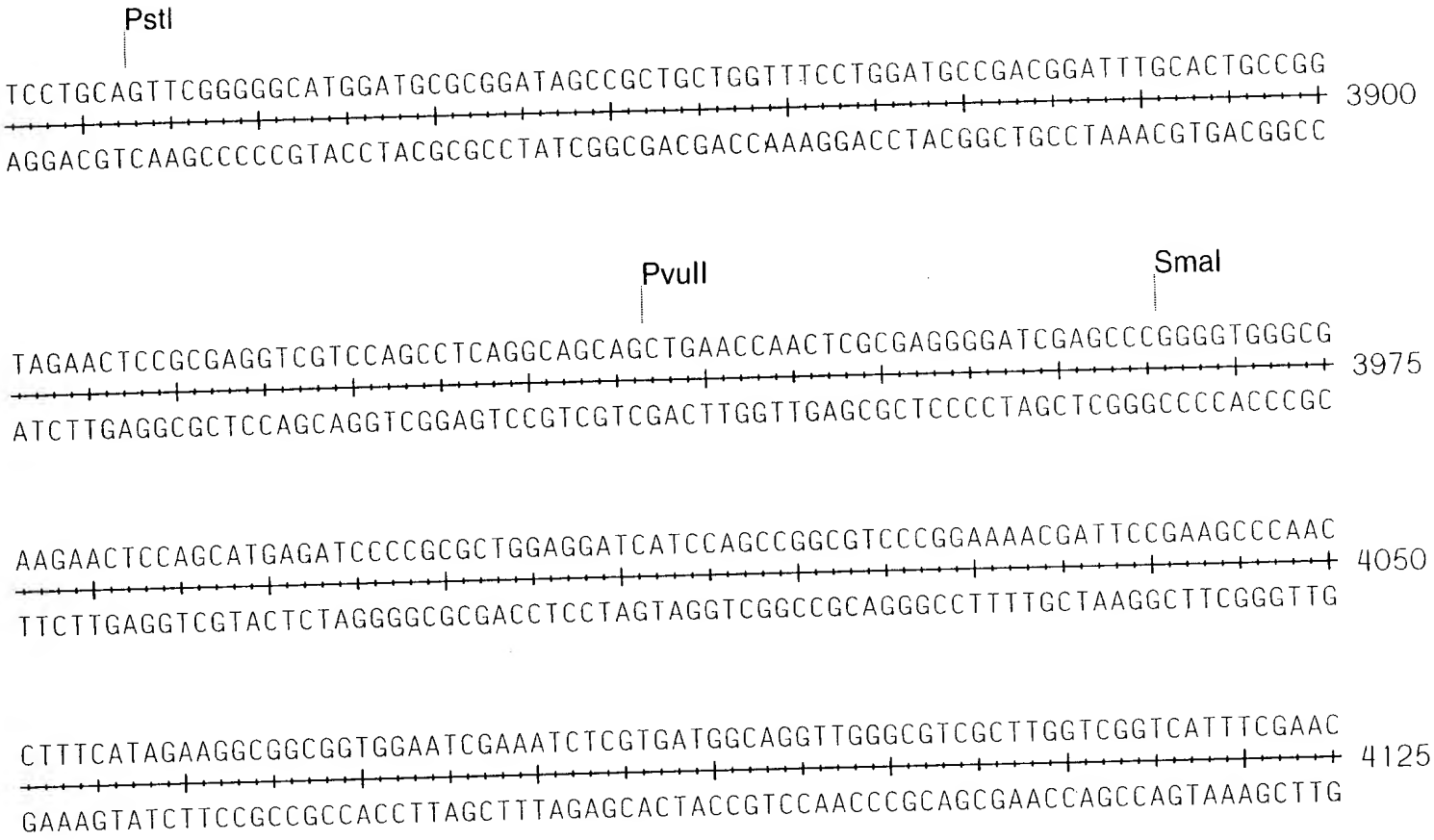


FIG.31P

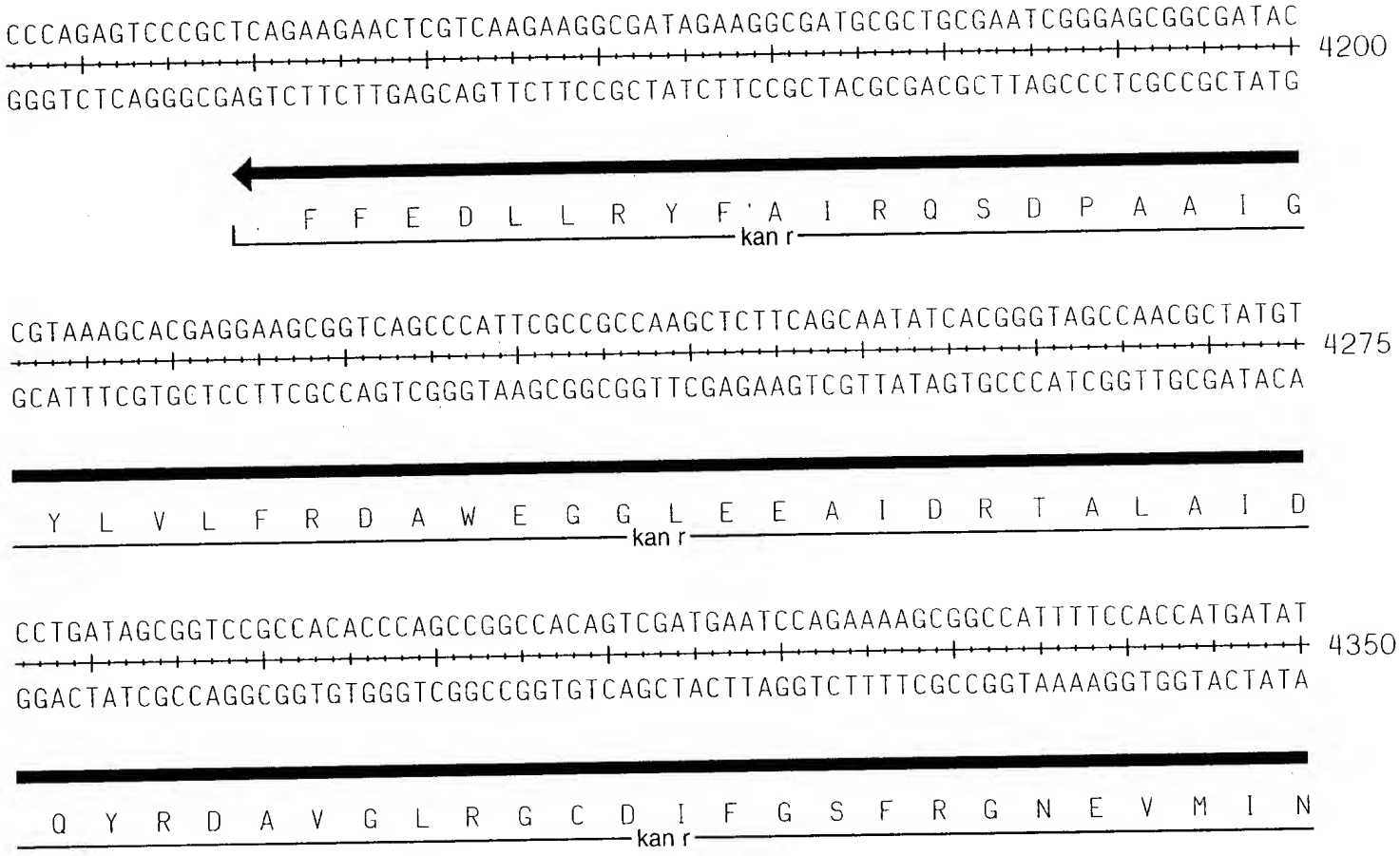


FIG.31Q

FIG.31R

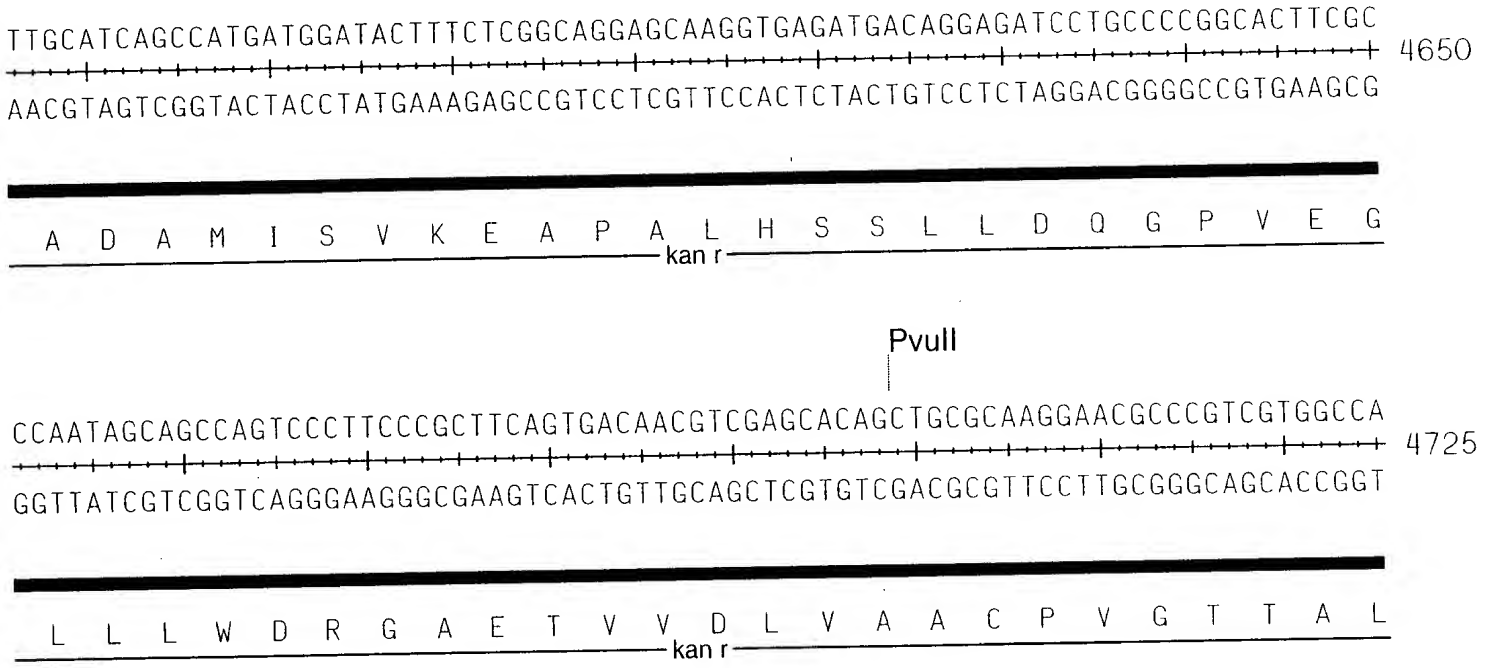


FIG.31S

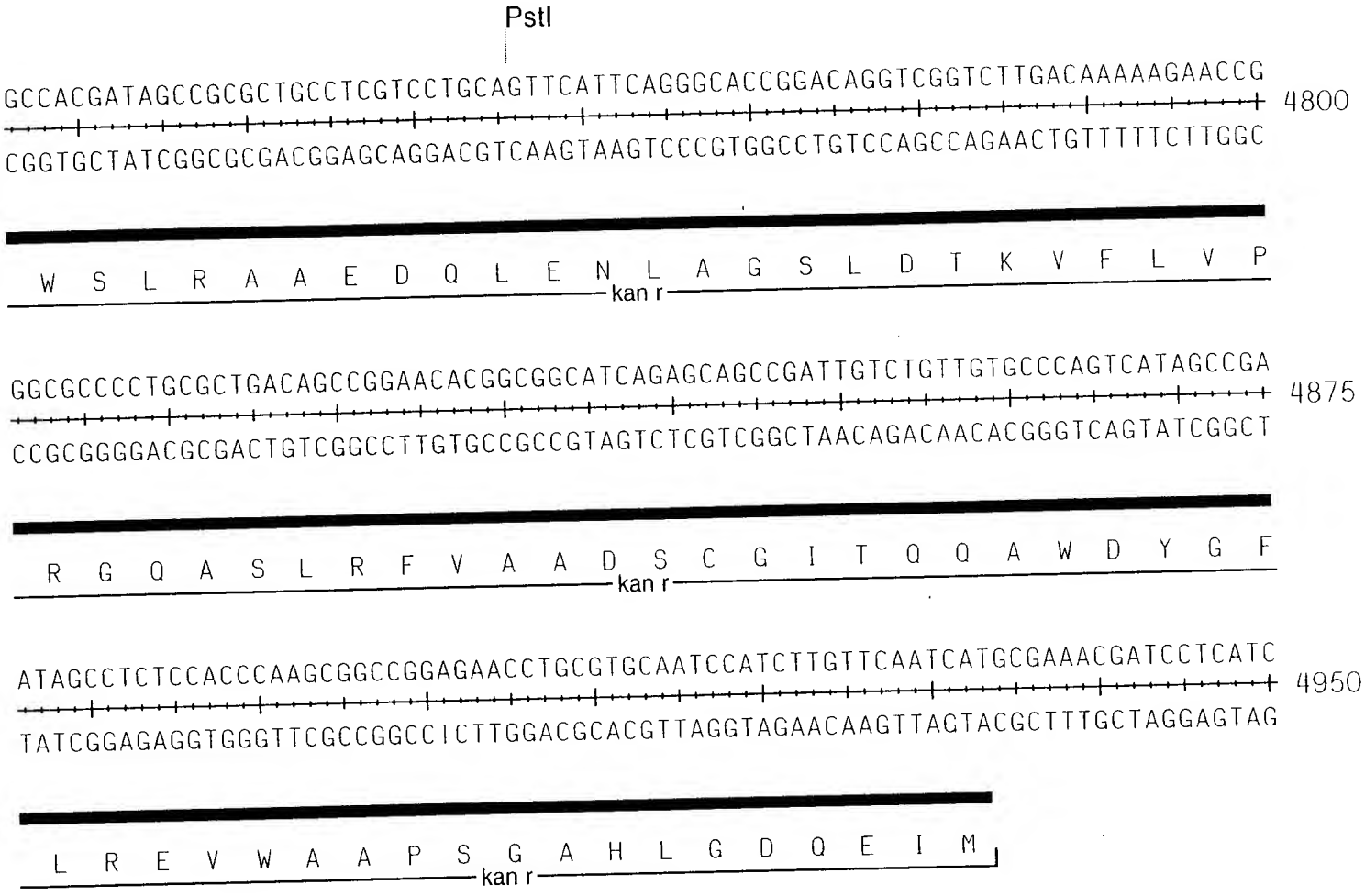


FIG.31T

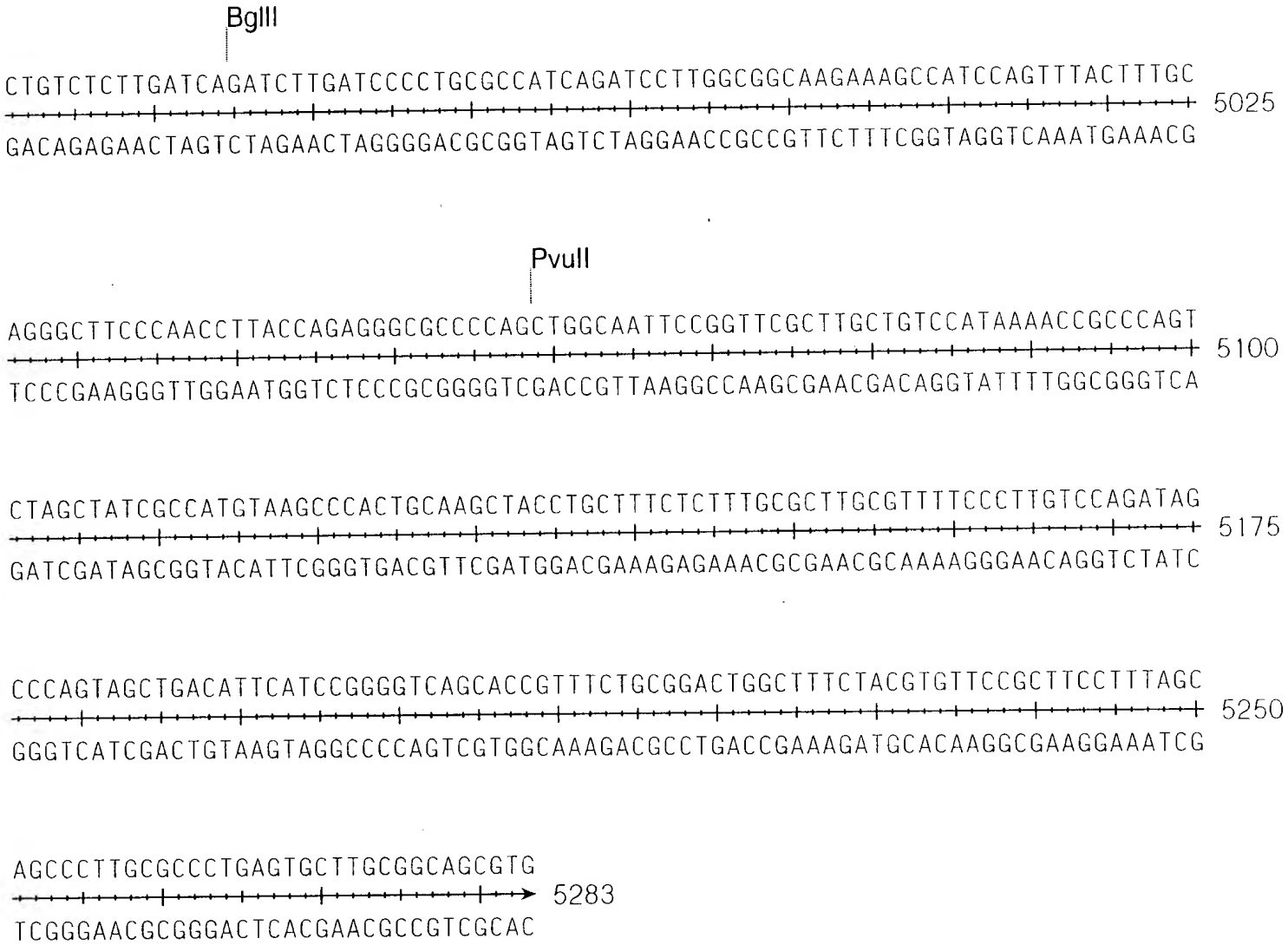


FIG.31U